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The Endocrine Glands in Obstetrics and Gynaecology

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THIS is indeed a most difficult subject with which to deal. It is still enshrouded with mystery. The anatomy of the glands of internal secretion is reasonably well understood, but their physiology is by no means clear. It is not likely that the pathology of these glands will be satisfactorily worked out until their physiology has been clarified. Hence we must not expect to have a very clear knowledge of their therapeutics until we better understand their physiology and their pathological states.

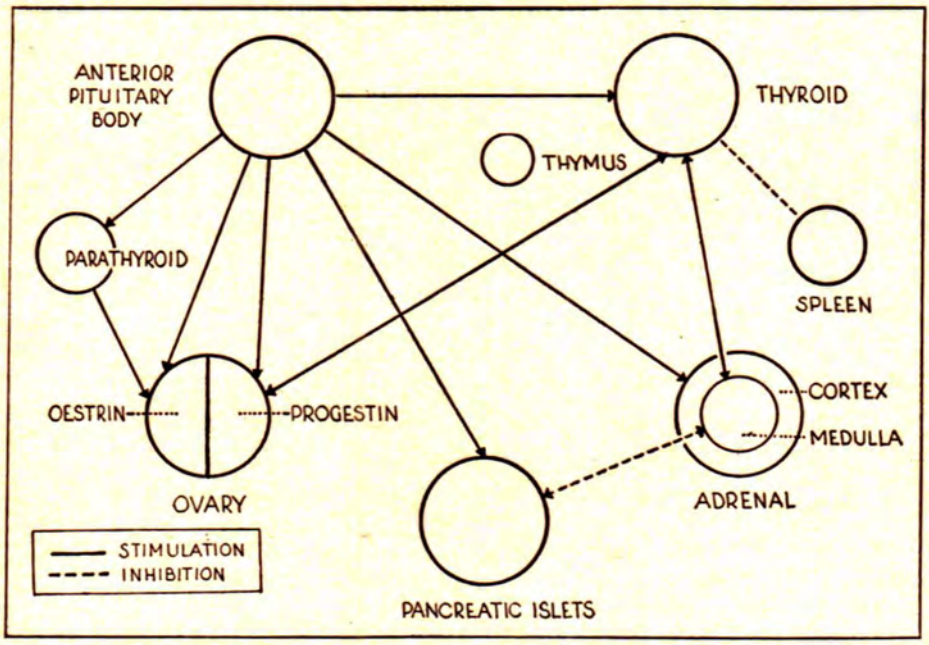
However, time and research work will doubtless gradually clarify this complicated field of the endocrines. In the meantime we must be content with the wonderful achievements already made, and keep a constant eye on the worthwhile assistance we are receiving. Our chief task is to sift out the few kernels from the chaff and make the best possible use of what we have at our disposal. Doubtless we are all using some of the glandular products without much success. Unless we insist on ourselves being meticulously careful in the selection of both the patient and the glandular product which we will use for a particular case, we will continue to have poor results and glandular therapy will fall more and more into disrepute.

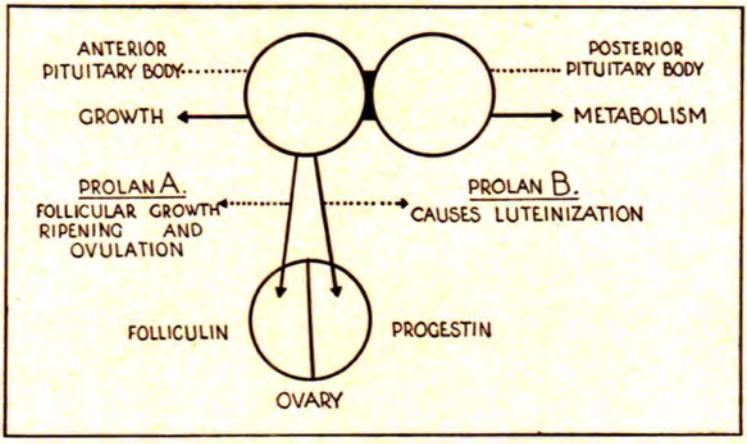
Therefore I attack this subject with temerity and extreme caution. I must at the outset be most careful in either condemning or acclaiming the merits of any of these glandular substances. I will endeavour to crystallize the whole subject to the best of my ability, and at the same time I will be dealing only with the obstetrical and gynaecological aspects of the subject.

I propose to divide the subject into the following categories:

(a) A review of the physiology of the glands.

(b) The common pathological conditions which are seemingly intimately associated with the glands of internal secretion.





The hormones of special interest in obstetrics and gynaecology are:

1. Three anterior pituitary hormones:
   (a) Prolan A—which stimulates follicle ripening and ovulation.
   (b) Prolan B—which stimulates luteinization of the follicle.
   (c) Prolactin—which stimulates lactation.
2. The two ovarian hormones:
   (a) Oestrin or folliculin which stimulates activity in the endometrium. This hormone arises from several sources.

(b) Progestin or the corpus luteum hormone which has something to do with the early implantation and development of the ovum. It is derived from the corpus luteum, the placenta, and perhaps also from the adrenal gland.

Folliculin or oestrin causes follicle-ripening. Progestin or the corpus luteum hormone completes the work begun by folliculin and prepares the endometrium of the uterus for the implantation of the ovum. It inhibits the formation of follicles, and causes swelling of the breasts at the onset of the period. Progestin completes menstruation and brings about ovulation. If conception does not occur, the corpus luteum decreases in size, and another follicle ripens. The follicle-ripening process reaches its height when the ovum is discharged, which is usually between the twelfth and fourteenth day, following the first day of the last period. The uterine mucosa has undergone the preliminary proliferative changes necessary to prepare it for the action of progestin. After the rupture of the follicle and the beginning of the corpus luteum, the secretion of folliculin is continued by that structure. As soon as the corpus luteum begins to develop, progestin is produced, and the typical progestational changes occur in the uterine mucosa. The glands are tortuous and the blood vessels dilate. The superficial stroma cells enlarge and look like the decidual cells of pregnancy. The uterine mucosa is now in the predecidual stage. If conception occurs the corpus luteum enlarges and its influence persists. If conception does not occur, the corpus luteum decreases in size and its influence diminishes, and menstruation occurs. Another follicle ripens and the cycle continues.

3. The anterior pituitary-like hormone, which accounts for the Aschheim-Zondek reaction. It arises from the chorionic epithelium, and is found in the urine of pregnant women.
4. Two hormones from the posterior pituitary gland:
   (a) Oxytocin which stimulates uterine contractions.
   (b) Pitressin which increases the blood pressure, stimulates peristalsis and inhibits diuresis.

Biological Classification of the Hormones:

1. Purely male or female hormones:
   (a) Progestin is a purely female hormone.
2. Partially bisexual hormones:
   (a) Hormones with chiefly male properties — androsterone, testosterone, propionate, androstenediol.
   (b) Hormones with chiefly female properties — oestrone and oestradiol.
3. True bisexual hormones — transdehydroandrosterone, testosterone, androstenediol.

THE TWO OVARIAN HORMONES

These are known under different names, but are commonly known as: (1) Oestrogenic substances, (2) Progestin.

The oestrogenic substances are also known as the female sex hormones, folliculin, theelin, amniotin, menformon, progynon, etc. These

substances are found in mature graafian follicles, in the urine during pregnancy, and in huge quantities in the urine of pregnant mares. The oestrogenic substances are also found in the testicles and in the urine of men, hence this hormone is not truly a female sex hormone. The oestrogenic substances are also found in various plants and are therefore *not* truly even a sex hormone. They are hormones of *proliferation*.

Oestrogenic substances are stable, and are resistant to light, heat and acids. They may be given by mouth, hypodermically, per vagina or per rectum. The hypodermic route is the surest. To produce the same effect by mouth, it is necessary to give from five to ten times as much as is given hypodermically. The dose of oestrogenic substances necessary to produce certain effects in animals is not a very accurate guide for the dose necessary for man.

The chief clinical uses of oestrogenic substances are for the relief of distressing symptoms of the menopause, gonorrheal vaginitis in children, some cases of hypoplasia of the uterus, senile vaginitis, pruritus vulvae, premature babies, and special cases of amenorrhoea.

Progestin is found almost exclusively in the corpus luteum, but some occurs in the placenta. It is not stable, being affected by light and heat. It should be preserved in a dark cool storage place. It is a lipoid and is soluble only in oil and is given intramuscularly.

The dose of progestin is usually expressed in Corner-Allen, Clauberg or Knaus units. In America, the Corner-Allen unit is used, while in Germany the Clauberg or Knaus unit is used. The Corner-Allen unit is arrived at as follows:

Corpus luteum extract is injected over a period of five days into a sexually mature doe castrated eighteen hours after mating. The Corner-Allen unit is the minimum quantity of progestin which produces on the sixth day a state of the uterus equal to that of the eighth day of a normal pregnancy. The Clauberg unit is measured in the same way as the Corner-Allen unit except that 600 gm. rabbits are used and are primed with oestrin before the progestin is given. A Knaus unit is the smallest amount of progestin necessary to protect the myometrium of a rabbit completely against large doses of pituitary extract. One Knaus unit is about one-fifth of the Clauberg unit. The basis of Knaus' test is his contention that the uterus contracts spontaneously and responds to pituitary extract during the first sixteen days of the menstrual cycle, but ceases its activity after this. He claims the uterus fails to respond to pituitary extract after the sixteenth day because of the presence of the corpus luteum hormone.

The chief clinical uses of progestin are in threatened and habitual abortion, dysmenorrhoea, and functional uterine haemorrhage. It has a relaxing effect upon the uterine muscle. Some cases of abortion are probably due to the deterioration of the corpus luteum during pregnancy, following which the posterior pituitary hormone, oxytocin, is permitted to act.

The two ovarian hormones here described have no direct action on

the ovaries. *No hormone seemingly has any effect on its parent gland.*

In treating cases of amenorrhoea of functional origin, we use the oestrogenic hormone for the first 14 days, and progestin after that. This treatment is substitutional, and usually requires repetition in order to keep the patient menstruating.

The gonadotropic hormones of the anterior pituitary gland are called prolan A and prolan B. They act on the ovaries only. They have no effect on a castrated individual; prolan A stimulates the development of follicles and prolan B produces luteinization.

Prolan is found in the anterior pituitary glands of both females and males. Enormous quantities are found in the blood and urine of pregnant women. After the third or fourth month of pregnancy the placenta begins the production of prolan.

Prolan is very unstable. One unit of prolan is defined as the minimum quantity necessary to provoke precocious puberty in infantile mice in five days. Prolan is used intramuscularly.

Prolan A produces ovarian follicles in young mice, and prolan B causes haemorrhages into the follicle. Such an effect, following the injection of pregnancy urine into an immature female mouse, is interpreted as a positive Aschheim-Zondek test. **If only ovarian cysts result** there is *no* ovarian function. Thus the Aschheim-Zondek test may be used to detect the presence or absence of ovarian function. When the ovaries cease functioning the anterior pituitary produces an excess of hormones.

Clinically prolan is used to stimulate the growth of the uterus in cases of hypoplasia (through the ovaries) and also for the treatment of women with profuse menstrual bleeding. As yet there is no preparation which contains only prolan A or prolan B. Most preparations contain a preponderance of prolan B. It is cheaper to give prolan than progestin for stimulating the endometrium.

In considering the use of hormone therapy in clinical conditions associated with glandular dysfunction, it is wise to remember,

(1) that there is a great discrepancy between laboratory knowledge of the hormones, and their clinical application, and
(2) that the preparation should only be used after a careful study of each patient's requirements.

The common pathological conditions which are associated with glandular dysfunction may be considered as follows:

1. *Delayed Puberty.* In this condition, the associated constitutional disturbances should be treated primarily. The glandular substances which may help are thyroid extract, along with oestroform and progestin. Oestroform is given intramuscularly in order to stimulate follicle-ripening and then progestin is given for luteinizing purposes. This method may have no effect or it *may* start off menstruation, which usually will not continue unless the treatment is maintained. Progynon B is also used for these patients. Progynon B (Schering) is given in

doses of 50,000 international units followed by daily injections of Prolution (Schering) for five or six days.

2. *Dysmenorrhoea.* In certain cases, where the etiology is believed to be endocrine in origin one may try hormone therapy. Some cases may be due to a deficiency of progestin. For these cases a series of four to eight injections of 100 rat units given on alternate days may be given during the second half of the intermenstrual period. This therapy is repeated monthly for four or five months. The therapy is sometimes of value.

3. *Functional Uterine Bleeding.*

(a) Excessive bleeding of endocrine origin in the teens is usually difficult to treat. The cause of this bleeding is usually an excess of oestrin and a dearth of progestin. Treatment consists of using the anterior-pituitary-like hormones, such as Antuitrin S, follutein and A. P. L., along with an extract of the anterior pituitary body. An investigatory curettage should be done before starting treatment.

(b) Metropathia Haemorrhagica.—A diagnostic curettage must be done at the onset. Treat this condition with a pregnancy urine extract, using a daily dose of three to seven hundred rat units —an average of five hundred rat units daily.

(c) Functional Menorrhagia.—Thyroid extract may be used, if it is indicated, along with the luteinizing hormone of the anterior pituitary.

(d) Hypomenorrhoea.—Try thyroid extract, if it is indicated, along with an oestrogenic hormone. They are sometimes effective, when used in conjunction.

4. *The Menopause.* Oestrin usually relieves the vaso-motor phenomena of the menopause. Emmenin often gives results also. Excessive flowing at this time is usually associated with metropathia haemorrhagica and the treatment of this condition was outlined above.

5. *Pruritus Vulvae.* This condition often subsides when the patient is given oestrin.

6. *Migraine.* At times migraine symptoms yield to the use of Progynon B in oily solutions.

7. *Painful Breasts.* These are not helped greatly by endocrine therapy. Some cases, however, are helped, it is claimed.

8. *Frigidity.* Some cases of frigidity may be helped with Progynon B (Schering).

9. *Infantile Gonorrhoeal Vaginitis* is often helped considerably with Progynon B in oil, using 5,000 international units every other day for a period of eight weeks.

10. *Threatened Abortion.* Some cases, particularly of the habitual abortion type, may be helped with Prolution (Schering), using 1/25 to 1 international unit doses.

11. *Leukoplakia.* Leukoplakia will occasionally yield quite satisfactorily to treatment with the oestrogenic hormone.

12. *Sterility.* An occasional well-chosen case of sterility may receive some assistance from treatment with progestin.

SUMMARY

1. Our knowledge of the physiology, pathology and therapeutics of the endocrine glands is enshrouded in mystery at the present time.
2. There is a great discrepancy between laboratory knowledge of the hormones and their clinical application.
3. Hormone therapy has been and no doubt will be greatly abused until we know much more about it.
4. Generally speaking, hormone therapy gives the best results when used in what appears to be a fairly healthy patient. The thin, undernourished patient does not respond as well to the hormone therapy as the robust patient.
5. Chemically, the female and male sex hormones are related, and their physiological effects are proving to be somewhat similar.
6. Long continued use of an oestrogenic hormone in young women or girls may not be *harmless*, and such prolonged treatment is not recommended until this problem has been clarified.

ABSTRACTS

A CASE OF ENDOMETRIOSIS: CONSERVATIVE TREATMENT FOLLOWED BY PREGNANCY

By A. CLAYE

Clin. J.; 47:75, 1938

The author reports the case of a woman, 30 years of age, married nine years. Her complaints were sterility, dysmenorrhoea and dyspareunia. Physical examination revealed an indefinite mass behind the uterus, but no signs of gonorrheal infection. At operation the left ovary was found to contain a large chocolate cyst, while the right ovary contained a few small cysts. The left ovary was removed and a wedge resection of the cyst-containing area of the right ovary was performed. The patient made an uneventful recovery, her symptoms were relieved and she subsequently became pregnant. Two other cases of conservative operation for endometriosis followed by pregnancy are reported, and the author believes that pregnancy in these cases is not so rare as commonly supposed. He believes that in any patient in whom the endometriosis is of only moderate degree an attempt should be made to preserve some of the ovarian tissue so that conception would still be possible. The author also states that he believes the age period for endometriosis is not as high as commonly supposed, as he has seen a considerable number of cases under 30 years of age.

—N. ENGLAND, '39.

THE USE OF INSULIN IN URTICARIA

By W. CAVEN

Can Med. Assn. J.; 38:459, 1938

Two cases of urticaria were reported which showed remarkable improvement when treated by the injection of five units per day of either the regular or protamine zinc insulin. The mode of action of the insulin in these cases is not understood, but it is a simple and safe treatment in intractable cases of urticaria and allied conditions.

—R. YOUNG, '39.

Functions and Disorders of the Thyroid Gland

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INTRODUCTION

OUR knowledge concerning the structure and functions of the thyroid gland has accumulated slowly for over two hundred years, following the first anatomical description of the organ by Wharton in 1656. The discovery of iodine in the gland by Courtois in 1812, together with proof of its presence in sea sponge, which had long constituted a traditional and partially successful method of treating cases of simple goitre, paved the way for the more recent and rapid strides towards understanding the fundamental role of the thyroid in iodine metabolism. Much of what is known today has grown out of studies of simple goitre. In the days of Kocher, when operative interference was indicated on account of pressure symptoms, it was customary to perform a total thyroidectomy. The subsequent events in these patients brought to light the clinical consequences of thyroid deficiency, often at first complicated by unwitting removal of the parathyroids. From this foundation, there speedily grew up an appreciation of conditions due to pathological hypothyroidism. Experimental work led to discovery of the possibility of making good the thyroid insufficiency by the administration of thyroid by mouth, or parenterally. The influence of the thyroid on nitrogen metabolism, on gaseous exchanges, and on many other activities, was gradually appreciated. Replacement therapy was carried on, to the point of inducing in normal animals and man a state of hyperthyroidism, from which an understanding of certain clinical states has steadily developed.

The present century has seen great progress along many avenues. The gross and microscopical anatomy has been the subject of detailed study, revealing certain definite changes associated with fluctuations in the functional state of the thyroid. Accurate biochemical estimations have indicated a parallel between the iodine content of the gland and the histological picture (Marine). Increasing investigations of all aspects of iodine metabolism has shed much light upon the various types of goitre, the factors causing them, the nature and mode of action of the active principle of the thyroid, and other problems of prime importance. With the indefinite boundary line between physiological extremes and abnormal conditions of the thyroid, growth of knowledge of the normal influences has accompanied investigation of the many pathological conditions. Study of all of the normal and abnormal phenomena of the vital processes of the body has facilitated a better appreciation of the influence of the thyroid gland in various directions, and of its essential place in the economy of the organism. Its intimate relationship to other

endocrine organs is apparent. Its regulating action in connection with metabolism, and its importance in connection with growth and proper development and maintenance of normal physical and mental well-being are among the aspects along which research has yielded valuable information already. Numerous problems still await solution.

ANATOMICAL FEATURES

The thyroid gland consists of glandular elements or vesicles, grouped together to form many incomplete lobules which are loosely bound together by areolar tissue. The connective tissue partitions contain the vascular and nervous structures of the gland. The whole is invested by a strong capsule. The glandular units may be pictured as hollow balls containing the secretion or "colloid" which is enclosed by a single layer of secreting cells. The latter are described usually as being cubical in type. It is now established that the shape and size of the epithelial cells, their contents (type of granules, staining properties, etc.), and the character of the alveoli vary markedly and distinctively in accordance with the particular phase of secretory activity existing at the time.

Hyperplasia is characterized by marginal vacuolation and later disappearance of colloid. The cells become columnar in shape and elaborate changes in the number, size, disposition and staining qualities of the various intracellular bodies and the Golgi apparatus are usual. The alveolar walls become infolded and crinkled, the vascularity is greatly increased and in some cases there is an increase of lymphocytes, presenting a lymphadenoid appearance. The histological picture is largely made up of epithelial cells, surrounding irregular chinks containing a small amount of pale colloid; the contrast with the usual resting picture of low cells, more or less uniform circular or oval acini, and plenty of deeply staining colloid everywhere, is most striking. Some degree of variation is exceedingly common, for the thyroid is sensitive to all manner of influences, including demands for its active principle on one hand and supplies of certain substances on the other hand; additional factors operate by way of the blood stream or sympathetic nervous system.

Subsidence of hypertrophy and hyperplasia, or involution, involves an opposite series of changes. In all glands, these processes have alternated many times, and residual evidences of the past cycles may be visible. There may be areas of hyperinvolution, where the process of regression has progressed beyond the normal, the cells have become flattened, the vesicles are grossly enlarged and contain excessive colloid; there is a marked relative avascularity.

The thyroid gland is very richly supplied with blood. Besides ministering to the various local metabolic requirements the blood stream conveys raw materials to the gland, and also some substances which affect its activity in various ways. This is likewise the path whereby the thyroid principle is carried away and distributed to the body tissues. On theory alone, therefore, one would expect that the sphere of influence

of the gland might be as widespread as the field of living cells supplied by the vascular flow. No doubt this is the case, although our powers of discrimination are inadequate to prove the point. The thyroid possesses a rich plexus of lymphatics, passing through the stromal partitions, and draining to nearby glands of the deep cervical system.

The nerve supply of the thyroid appears to be derived solely from the cervical sympathetic system. There is an extensive outflow from the middle and inferior ganglia, reaching the gland as a perivascular plexus along the coats of the corresponding arteries. The non-medullated fibres establish perifollicular plexuses within the gland substance. Neurofibrillae have been described extending to special terminations in immediate contact with each epithelial cell. There is much evidence supporting a connection between thyroid overaction and apparently primary disordered states of the autonomic nervous system; this has been stressed by Crile and many others. Cannon regards the above as true secretory nerves to the thyroid. The normal control exerted by this nervous factor is still somewhat problematical; however, it is well to keep in mind that there is here an important pathway, with vast potentialities for weal or woe.

METHODS OF STUDY

The following paths of research have been employed in studying the thyroid gland:

1. *Anatomical Studies.* These have been outlined already, revealing that highly characteristic alterations distinguish the different phases of functional activity, and provide an accurate gauge of the degree of the latter.

2. *Biochemical Investigations.* These cover the entire subject of the metabolism of iodine, and the intimate relation of this element to the thyroid. Marine has shown that hyperplasia develops regularly whenever the iodine content of the dried thyroid tissue is less than 0.1 per cent. The cause for this may lie in deficiency of exogenous iodine, or in defective utilization of iodine. The relationship of simple goitre to iodine insufficiency is most definite, although many other factors take part, and the relation is not absolute.

The isolation of three distinct iodine-containing compounds from thyroid tissues, by different methods of hydrolysis and extraction, has gone part way in solving questions appertaining to the synthesis of the active principle in the gland, the steps concerned, the path of discharge into the blood, etc. The physiological activity of thyroid tissue is proportional to the total iodine present. The latter (for which thyroid has a most peculiar affinity) exists in the following compounds: iodothyroglobulin is present, as such, in the gland; diiodotyrosine, which is inert in the pure form, but becomes active when combined to form thyroxine; thyroxine, which qualitatively, but not quantitatively, is equivalent to whole gland in most respects. Thyroxine has been synthesized chemically by Harington.

The interchanges between these compounds is too speculative to merit reference here. The exact nature of the active secretion still defies certainty. Attempts have been made to distinguish the paths taken by the principle, and its precise locus of action. Some evidence warrants the supposition that fine nerve terminals provide the channel whereby the principle reaches the interior of the various living cells, and that at this point a profound influence is exerted upon the anaerobic phase of tissue oxidations. No final conclusions are possible in the present state of our knowledge. This view would satisfactorily account for the known latency of action of thyroxine.

3. *Experiments in Vitro.* These have proven that no thyroid preparation has any effect on isolated, perfused tissues as regards the respiratory exchanges, acceleration of heart rate, etc. However, when corresponding tissues are taken from an animal which was treated with thyroid for a time preceding death a very definite response is obtained. The inference is, that the effect is peripheral, that it occurs in a wide variety of living tissues, that it is dependent upon access of the thyroid principle to the cells in the body, and that the outstanding action appears to be an acceleration of oxidative processes.

4. *Hypothyroid States.* These occur in human beings as a result of pathological thyroid insufficiency or following too radical operative removal. In animals, the condition is produced experimentally by extirpation of the thyroid. Various grades occur in keeping with the proportional lack of functional gland tissue. The clinical and pathological results vary considerably according to the age of onset of the deficiency. When it dates from birth, as in children of goitrous parents in iodine poor districts, the result is a cretin. In these, physical and mental development are grossly incomplete. The cardinal abnormalities include markedly subnormal metabolism, underdeveloped genital organs and functions, gross mental deficiency, specific changes in the skin, and commonly a goitre. Deaf-mutism is frequently seen.

When the hypothyroidism commences in later life, the effect on growth and mental development depends upon the time of onset, the degree of thyroid want, and other factors. The condition has been designated "myxoedema" which is characterized by a depression of all the vital processes of the organism, with a slowing down of the metabolism and diminished excitability of the vegetative nervous system. Trophic disturbances affect the skin, producing epidermal thickening and scaliness, and a deposition of mucinoid material in the deeper layers of the skin; there is a deposition of fat with a predilection for certain areas. The hair becomes brittle and falls out, and the nails and teeth develop abnormally. Cerebration is slow.

In the young there is a delay in skeletal development; mental advancement is interfered with, giving a subnormal I. Q. To some of these cases of early commencement of a subthyroid state the name "infantile myxoedema" has been attached.

In all of the hypothyroid conditions the basal metabolism is low, the gaseous exchanges are diminished, and nitrogen excretion is reduced. The output of water, salt and calcium is likewise low. The glucose tolerance is increased. Hypothermia is customary. Anaemia and early development of arteriosclerosis are frequently seen. The entire picture is that of depression of every vital process capable of accurate estimation.

5. *Substitution Therapy.* This refers to the possibility of making good artificially the defect in secretion of the thyroid gland. This has been done effectively by the oral ingestion of whole thyroid or its iodine-containing compounds, by injection of certain products, notably thyroxine, and by grafting procedures. In all cases it has been proven beyond doubt that regular maintenance of an adequate supply of the essential principle will effect and maintain a return to a relatively normal state. However, an early start is necessary, especially to produce a normal mentality in cretins. Physical development and the various metabolic processes are more readily susceptible to therapy. The excess and abnormal tissue is removed, with a reduction of weight. The skin regains its normal texture, color and appearance, and its appendages grow normally once more. The mind clears. Sexual function improves. The metabolic activities speed up in all respects. Clinical results have been brilliant, but careful supervision is advisable at all times during treatment.

6. *Hyperthyroid Conditions.* These arise under various circumstances. They occur clinically whenever a hyperplastic gland pours out an excess of active principle into the circulation irrespective of the needs of the organism (Kocher has spoken of this as "diarrhoea" of the gland). Recently, it has been possible to produce this state experimentally by administration of anterior pituitary preparations containing the thyrotropic hormone. Occasionally, thyroid secretion produced by metastatic carcinoma from the thyroid may be the cause. The administration of exogenous thyroid to a normal man or animal, or of large doses to subthyroid individuals, will evoke the distinctive features; hyperactive grafts have the same effect.

Whatever the cause, the picture is that of a machine which is speeded up. The changes affect all parts of the body and are directly opposite to most of those listed under hypothyroidism above. The nervous system as a whole is particularly affected. Disturbance of the central nervous system is apparent in the characteristic nervousness, emotional instability and fine tremor. Many evidences of stimulation of both components of the autonomic nervous system are visible. Thus there may be a whole series of "eye signs". The cardiovascular system shows a persistent tachycardia, a forcible apex beat in cases of any duration, sometimes a moderate increase of both systolic and pulse pressures, and various signs of vasomotor instability. There is a strong tendency to the development of auricular fibrillation, in long-standing

cases, especially in patients of advanced years. The skin shows typically a delicate aspect, increased temperature (subjective sense of heat as well as actual warmth), hyperactive sweat and sebaceous glands, and other changes in keeping with increased local nutrition and blood supply. Alimentary disturbances reveal themselves in excessive appetite ("The furnace is stoked with the drafts open."), and a tendency to true diarrhoea; salivation may be prominent, and vomiting may take place. Various respiratory alterations may manifest themselves, e.g., irregular or rapid rate, inability to expand the chest normally or to hold the breath as long as usual; sometimes dyspnoea and cough of various types may appear. There may be menstrual alterations in women, and defective sexual function in both sexes.

Metabolism is significantly affected. The basal metabolic rate is almost invariably increased. As a rule, an accurate estimation of this figure is a reliable index of the severity of any hyperthyroid state, and closely parallels the pulse rate, clinical severity and the microscopical changes in the thyroid gland itself in true hyperthyroidism. Carbohydrate metabolism is altered in the direction of diminished glucose tolerance, sometimes with hyperglycaemia and even glycosuria. A relationship to true diabetes mellitus is not established except that hyperthyroidism may be an exciting cause of diabetes in an individual with a predisposition to this disorder. The output of nitrogen increases, as does that of salt. Calcium and phosphorus are eliminated in excess, with a resultant rarefaction of bones. Loss of weight shows greater utilization of fats. The level of the blood cholesterol is reduced so commonly that it has been regarded as a valuable criterion of the degree of hyperthyroidism; it is a less accurate indicator than increased blood cholesterol in hypothyroid states. Hyperthermia may accompany the high general metabolism.

In the young, growth is arrested with early closure of the epiphyses, and cell differentiation and specialization throughout the organisms are imperfect. These changes indicate the important role played by the thyroid in the fundamental processes of growth and activity in the living body.

All of the above effects can be removed, and a more or less full return to normal can be effected by withdrawal of the excess thyroid administration or removal of an adequate portion of the functioning tissue. Of course, certain changes occurring during the phase of development are not susceptible to treatment after permanent skeletal and other alterations have become evident.

7. Moderate doses of thyroid tissue or active preparations, insufficient to produce clinical hyperthyroidism, have been tried on experimental animals and man. In the main the changes have been lesser degrees of those outlined in the last section. Certain special tests merit passing mention, as those based upon oxygen-consumption, others dealing with a decrease of growth rate and the production of hypertrophy of certain organs in immature rats, and the acetonitrile test referring

to the protection afforded to mice against methyl cyanide. These and other special reactions serve a useful purpose in demonstrating the potency of various thyroid derivatives. The most reliable criterion of effectiveness is the relief of established hypothyroidism by graduated and controlled thyroid medication.

8. Detailed studies of the condition of *endemic goitre* have added much to our knowledge of certain problems. The geographical distribution has long been known to indicate much more than a chance relationship to a relative deficiency of iodine in the soil, water and produce of these areas. That the iodine intake in such districts is in reality unusually small is attested by the fact that the urinary output of iodine is low as compared with non-goitrous zones. Nevertheless, dietary iodine-shortage is not the only factor concerned.

McCarrison regards iodine-deficiency as by far the most noteworthy "negative agency"; other lesser important members of the group include vitamins A and C, protein, and phosphates, lack of any of which may have a bearing in the genesis of goitre. The presence of these in adequate amount, and especially iodine, may be pictured as shielding the thyroid against certain positive goitrogenic agents; conversely, want of any may be looked upon as lowering the threshold, or resistance, of the thyroid to these positive factors. The latter agencies comprise excess fats and fatty acids, lime as found in many waters, some substance found particularly in cabbage and believed to be cyanide liberated by a glucoside, insanitary conditions, and a number of others. McCarrison has shown that these are capable of summation, minor degrees of several factors in combination increasing the incidence of goitre experimentally in animals.

This view is no more than a hypothesis at present, although it can account satisfactorily for the observed facts. According to it, iodine-lack is the major factor in determining the endemicity of goitre, while the actual incidence is attributable to the other causes; hence the total absence of any fixed relation of iodine-deficiency and goitre throughout the world or in any district. Thus also is explained the astounding success that has attended the widespread prophylactic administration of iodine to animals and to school children.

So-called physiological goitre, where hypertrophy and hyperplasia occur at certain times of stress, notably at the sexual epochs in females, may be placed in the same group. Here it seems that calls for an increased output of thyroid secretion in the presence of a minimal iodine supply induce a true pathological picture of hyperactivity. In all of these cases of simple goitre, the irrational outpouring of active principle seen in hyperthyroidism is absent; when secretion is produced, it is stored as colloid and used in normal fashion.

In the discussion thus far, an effort has been made to indicate the chief influences activating the thyroid, and the local structural changes ensuing in the gland with their various physiological counterparts. At

the same time the probable nature of the active principle has been considered, as well as its distribution via the blood stream to living cells far and wide. The likelihood of a paramount locus of activity in the intracellular spaces has been touched on. Essential roles of the thyroid concerning various stages of development and at all times in the organism have been emphasized. It remains only to collocate the leading functions of the gland in order to clarify these. It must be clearly stated, nonetheless, that any separation of its duties into distinct compartments may be as mistaken as it is artificial. There are those who urge the view that the thyroid largely controls intracellular oxidative processes, and that all the apparently separate functions are actually compatible with this interpretation.

SUMMARY OF OUTSTANDING FUNCTIONS OF THE THYROID GLAND

(a) Metabolism.—

(i) Metabolism as a whole is stimulated, with increased production of heat, acceleration of all vital processes, and augmented elimination of nitrogen. Many findings favour the conclusion that this is probably the most fundamental of all of the general physiological effects of thyroid secretion.

(ii) Carbohydrate metabolism is influenced in the direction of more rapid breakdown of liver glycogen, with lowering of the sugar tolerance.

(iii) Oxidation of fats is increased throughout the body, with a tendency to wasting. The blood cholesterol is depressed in proportion (but not strictly) as the thyroid is overactive.

(iv) The metabolism of inorganic substances is affected. Thyroid activity intensifies mobilization of both calcium and phosphorus from bones, with exaggerated output of both; there is no hypercalcaemia in contra-distinction to the effects produced by the parathyroid hormone. Salt excretion is favoured.

(v) The metabolism and nutrition of the skin may perhaps be singled out for special mention; all tissues show the influence of the thyroid secretion, as the local blood flow, the activity of the sweat and sebaceous glands, the fat and water metabolism, and the development and characters of the appendages as well as of the skin itself.

(b) Heat Regulation is closely related to the metabolic level. The heat regulating mechanism shows instability in many conditions of thyroid disturbance; conversely, it is said that prolonged fevers cause a diminution of activity of both the thyroid and adrenal glands. Changes in body temperature have been found to affect directly the blood-flow through the thyroid and the oxygen consumption by its tissues. Subjective sensations of warmth and cold accompany the respective characteristic variations of general metabolism in hyperthyroidism and hypothyroidism, and to affect the tolerance for certain environmental and climatic conditions.

(c) Growth and Development are influenced in vital respects, in the mental sphere no less than the physical. This truth is exemplified dramatically by comparison of a cretin with a normal human being. The success attending timely and controlled exhibition of thyroid in the former group attests to its fundamental importance at all stages and in all processes of development. Cell differentiation throughout the organism appears to be very largely dominated by the thyroid principle. Experimental work already quoted has indicated its tendency to accelerate amphibian metamorphosis at the expense of quantitative growth. A comparable control of cell specialization in most or all tissues of all types of animal is supported.

(d) The Effects of Thyroid Secretion on Individual Tissues.—This subject has received considerable attention from time to time, especially as additional impetus was afforded by clinical observations implying a specific activation of certain systems in hyperthyroid states and corresponding deficient functional activity in hypothyroidism. It has been proved conclusively that the thyroid secretion has no direct action on isolated, perfused tissues, but that changes can be detected in the gaseous exchanges of tissues taken from animals treated with thyroid ante-mortem. Much evidence connects up the peripheral action of the thyroid with intact nervous pathways. The intimate relationship of the thyroid secretion with the autonomic nervous system, regarding tissues controlled by the latter, is established and has led to the view that the thyroid principle "sensitizes" various cells to the action of the sympathetic system in particular. The exact mechanism of this relation is not clear; the heightened level of intracellular oxidative processes occasioned by the thyroid principle might account for the facts in itself, the process being in no wise specific. Many problems still await solution.

(e) Interrelationships of the Thyroid with other Endocrine Glands.—This is a field of much uncertainty, beset with many inherent difficulties. It is almost impossible to determine accurately the basic facts. Clinical evidence is often obscure. Controlled experiments are complicated and few. Much speculation has surrounded the little established truth in the various writings. Relations are rarely if ever one-sided, but are reciprocal as a rule. Generally multiple interrelationships complicate any given picture. Many deductions are inadequate or even erroneous.

(i) The Anterior Pituitary.—The part played by the thyrotropic hormone of the pituitary in connection with thyroid stimulation has been outlined earlier in this discussion. This factor may operate in both physiological and pathological conditions of increased functional activity of the thyroid.

Conversely, hypo-function of the thyroid for any reason has been shown to lead to gross enlargement of the pituitary, especially of the intermediate and posterior portions, with recognizable histological changes. These structural alterations can be prevented

by administration of thyroid to thyroidectomized animals, or either thyroid or iodine to goitrous rabbits. This proves a direct action of the thyroid secretion on the hypophysis. It has been stated that prolonged thyroid feeding to normal animals leads to hypoplasia of the pituitary.

(ii) The Adrenal.—A. Cortex.—There is some evidence that an inhibitory relationship exists between the adrenal cortex and the thyroid: cortical hypo-function has been reported with hyperthyroidism, and administration of cortex or extracts thereof have benefited the latter state (Shapiro).

B. Medulla.—Any relation is probably peripheral, the thyroid serving in the capacity of activating agent.

(iii) The Islets of Langerhans.—The thyroid causes depletion of liver glycogen and diminished sugar tolerance. Sugar tolerance curves of hyperthyroid patients may be "indistinguishable in type from those of patients with mild diabetes". A very few workers believe that when prolonged, the thyroid effect may lead to true diabetes. This view is highly speculative.

(iv) The Thymus and thyroid are bound together in some ill-understood way. It is stated that removal of either causes hypoplastic changes in the other.

(v) The Parathyroids and thyroid both mobilize calcium from bones; the former alone raises the serum-calcium value. The former may possibly depress the excitability of the tissues to the sympathetic system. However, no certain relationship holds good.

(vi) The Gonads.—In both sexes some degree of sexual infantilism follows thyroidectomy in the young, while sexual depression is common in myxoedema. Menstrual functions in the female are closely related to thyroid activity; shortened and scanty menses accompany hyperthyroidism typically, while increased bleeding and duration of loss occur with hypothyroidism of degrees that are so minor as to be sub-clinical. Appropriate therapy, in the way of reducing the amount of functional thyroid tissue or thyroid administration respectively, will restore the menses to their status quo ante ordinarily. Recently it has been found that injections of oestrone in some animals will produce thyroid involution.

Anti-thyroid Compound.—There has been a revival of late of a belief that substances antagonistic to the thyroid principle may be developed in the blood or tissues of animals. On this assumption attempts have been made to confer what would be virtually a passive immunity to hyperthyroid patients. Published results and opinions on this matter are at variance. Proof of the existence of such compounds is lacking, and successful transference is highly doubtful.

It will be evident that the province of thyroid influence is as broad and vast as the distribution of living cells supplied with blood. Various functions can be separated and emphasized. When one reflects upon the utter dependence of all vital reactions upon intracellular oxidative pro-

cesses, it is obvious that by affecting these generally the thyroid must affect growth and development, and functional activity of muscles, nerve cells, and no doubt all other glands and tissues. It would appear certain that the same iodine-containing compound (or group of such substances), elaborated by the thyroid and designated active principle, is responsible for all of the distinguishable activities. No essentially different fractions have been separated. The details of a particular response will vary then according to the tissue and the local conditions, and not in any other qualitative sense.

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METABOLISM OF VITAMIN C IN RHEUMATIC FEVER

By J. RINEHART, L. GREENBERG, M. OLNEY AND F. CHOY

Archives Int. Med.; 61:537, 1938

The authors have been able to produce degenerative and proliferative changes similar to Aschoff nodules by injection of streptococcus toxin into scorbutic guinea pigs. Using the Farmer and Abt method of determining the cevitamic acid content of blood plasma, they found consistent low vitamin C content in cases of rheumatic fever. Infectious conditions such as tonsillitis and tuberculosis also showed low values but not as low as in rheumatic fever. Three factors may aid in producing these low values: a deficient intake of vitamin C, depletion by the disease or by a preceding infection, or an inherent or acquired metabolic fault. From experimental data, the authors conclude that vitamin C deficiency commonly exists in rheumatic fever, and is probably of etiological significance in the disease. Carefully controlled prophylactic and therapeutic studies are suggested.

—A. VOGELSANG, '38.

INSULIN THERAPY IN DEMENTIA PRAECOX

By R. MACKAY

Nova Scotia Med. Bul.; 17:221, 1938

Insulin treatment for dementia praecox was first used by Dr. Sakel of Vienna, who, in using insulin to stimulate the appetite noted a change in mental reactions. The author has been using the treatment for six months. The patient should be in good physical health, and respiratory infections are a contra-indication for the treatment, because of the tendency of insulin to produce pulmonary oedema. The patient is given one dose of insulin in the morning, but no breakfast during the treatment. The insulin is repeated every morning, in doses increasing by 10 units, until improvement results or coma develops. The treatment is discontinued during the menstrual periods. After stopping the treatment for a few days it should be started again with a smaller dose than the maximum dose which has been given. Fatalities vary from one to three per cent. About 30 per cent of cases are completely cured, while a similar number show an improvement. It is not known whether or not the cures will be permanent.

—D. WOLLIN, '39.

The Diagnosis and Treatment of the Tachycardias and Arrhythmias

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THE elucidation of the various types of tachycardia and cardiac arrhythmias forms a considerable part of the general practitioner's routine work. Many of these abnormalities of rate and rhythm lend themselves to diagnosis at the bedside when a careful examination is made. I propose to discuss the subject chiefly from the standpoint of diagnosis and appropriate treatment.

THE TACHYCARDIAS

Sino-auricular Tachycardia. Sino-auricular tachycardia is a regular, rapid heart action with normal mechanism at a rate varying between 90 and 180 beats per minute. The explanation of the increased rate is usually apparent. It is found accompanying fever, exercise, emotion, thyrotoxicosis and heart failure. It is a manifestation of neuro-circulatory asthenia. It may be due to certain drugs such as atropine. It is also found as a normal mechanism in certain healthy individuals. Heart disease is usually absent. The onset and offset of the attack are gradual. Auscultation of the heart reveals a rapid rate with a normal rhythm. Exercise increases the rate; rest or vagal pressure has the reverse effect. The therapy is directed toward the cause.

The Paroxymal Tachycardias. These disturbances have many characteristics in common. The pulse rate varies between 120 and 200, usually running about 160 beats per minute. The onset and the termination of the paroxysm are abrupt. The symptoms include palpitation, a "sensation of smothering," fulness in the neck, dizziness, fainting and occasionally precordial pain. During an attack many patients are exceedingly uncomfortable and show marked anxiety.

Paroxysmal Auricular Tachycardia is the most common type. Heart disease is usually absent, although the condition is frequently associated with mitral stenosis. The history frequently reveals previous attacks of a similar nature. The duration of an attack may be a few seconds, days, weeks or longer. The onset and the end of the attack are usually sudden, although the cessation may on occasion be gradual. Auscultation reveals a rate between 120 and 200 beats per minute. The rhythm is regular. There is no variation in the intensity of the first or second heart sounds. In certain instances, pressure over the carotid sinus or over the eyeballs effects a dramatic return to the normal rate.

Therapy, for the short attack, is not required. Many patients have learned through experience how to manage their own attacks. Such measures as holding the breath, forced expiration, drinking ice water, vomiting and firm abdominal pressure may prove successful. If simple

measures fail, pressure over the right carotid sinus should always be tried in an effort to restore the normal rate. The pressure should be maintained for a period of one minute. If pressure over the right carotid sinus is of no avail, pressure over the left carotid sinus may be resorted to. If unsuccessful, moderately firm pressure on either eyeball with the lid closed (oculo-cardiac reflex) may bring about the desired effect. In approximately 20 per cent of all cases, one or other of these measures will restore a normal rate. In the remainder, one must resort to drug therapy. Sedatives, such as bromides, luminal, chloral, and, rarely, morphine, are useful. Digitalis, strophanthin, quinine, quinidine and apomorphine are some of the drugs frequently used. Any one of these preparations may be effective in one patient but not in another. Mecholyl in doses of 40 to 50 mg. given subcutaneously almost invariably causes an abrupt cessation of the attack. I have used this drug repeatedly and, except for flushing, sweating, salivation, slight pressure in the chest and occasional vomiting, have observed no severe reactions. Syrup of ipecac is worthy of trial. The minimal effective dose for oral administration varies from one to four drams. An initial dose of two drams should be given, and, if no vomiting results or the desired effect is not obtained, the dose may be repeated in 50 minutes. After the administration of the effective dose, nausea and vomiting usually develop within from 15 to 50 minutes. At the same time the heart rate slows abruptly and the normal rate is restored. For the prevention of attacks, quinidine sulphate in rations of three grains two or three times a day is often effective.

Paroxysmal Ventricular Tachycardia, unlike the auricular variety, is generally associated with serious heart disease, particularly coronary sclerosis. It occasionally complicates acute coronary thrombosis. In such cases it may be transient; on the other hand, it may persist for several hours during which time the patient's life hangs in the balance. Recognition of this particular type of tachycardia is of great importance since proper therapy may prove a life-saving measure.

As stated above, in paroxysmal auricular tachycardia the rhythm is absolutely regular and the heart sounds have a constantly similar character. In contra-distinction, with the ventricular variety, careful auscultation reveals a slight, but distinct, irregularity, although the rhythm is essentially regular. In addition, the quality and intensity of the first sound at the apex usually varies with occasional heart cycles. The heart sounds for periods of several seconds may be identical, but suddenly either a clicking sound is heard, a "muffling," or an accentuation of the first sound takes place. The reason for this phenomenon is probably due to the varying time relations between auricular contraction and ventricular contraction. Carotid sinus pressure, or pressure over the eyeballs, has no effect on ventricular tachycardia. Jugular pulsation from the auricles may be noted at a rate slower than the auscultatory heart rate.

Since this variety of tachycardia is often the precursor of ventricular fibrillation and death, immediate treatment is imperative. Quinidine sulphate is the one and only effective drug. Depending on the patient's condition, it may be given by mouth or by the intravenous route.

THE ARRHYTHMIAS

Sinus Arrhythmia. Sinus arrhythmia is most common in young people, especially in children. It is due to vagal action on the sino-auricular node, which causes the pulse rate to wax and wane with respiratory movement. Auscultation reveals quickening of the rate with inspiration and slowing with expiration. The irregularity readily disappears with any increase in pulse rate such as that induced by exercise, fever and after the administration of atropine or amyl nitrite. In certain rare cases the phases of slowing and acceleration are independent of respiration and due to the phenomenon of a shifting pacemaker. For this irregularity no treatment is necessary.

Premature Beats or Extrasystoles. Premature beats occur when some portion of the heart muscle other than the normal pacemaker becomes irritable and initiates a stimulus which produces a contraction. The ectopic focus may be situated in the auricles, in the auriculo-ventricular node or in the ventricles. The extrasystoles are usually not associated with myocardial damage and are more frequently found with a slow rather than a fast heart rate.

The chief sign of a premature beat is its prematurity. This may be discovered by auscultation of the heart, palpation of the pulse, inspection of the jugular pulse, or a combination of all three procedures. Depending on the time relation of the beat, the pulse may be of the bigeminal, trigeminal or quadrigeminal type. Auricular premature beats are comparatively rare. They are usually not followed by a compensatory pause. Ventricular premature beats are common. They are almost always followed by a compensatory pause, so that the time pauses before and after the ectopic beat are together equal to the time interval between two normal beats. Premature beats have little significance when careful examination reveals no organic heart disease, but when there is evidence of cardiac disease they are of great importance. A classical example of the benign course which extrasystoles may take is that of Erb, the famous physician, who observed the presence of this irregularity in himself at the age of 29; during the next 27 years, it in no way impaired his mental or physical vigour. From the age of 56 to the age of 63 years, he was subject to attacks of paroxysmal tachycardia, which were disagreeable, but did not interfere very much with his work or with his favourite sport of mountain climbing. Subsequent to this, there were only occasional extrasystoles. At the age of 70, he underwent a severe gall bladder operation and died at the age of 83 from infective colitis.

The differentiation of premature beats from sinus arrhythmia and

various grades of partial heart block is relatively easy. The usual disappearance of premature beats after exercise distinguishes the marked arrhythmia induced by frequently recurring extrasystoles from the arrhythmia of auricular fibrillation which increases with exercise.

The treatment of premature beats depends on the underlying cause. There is no specific therapy and often the irregularity is unaffected by any form of treatment. Individuals who experience no discomfort require no therapy. In certain cases the ectopic beats give rise to great discomfort and alarm. The patient complains of a "thump" in his chest, a sensation as if the heart had turned over, or precordial pain which may radiate down the left arm, the so-called "extrasystolic" type of angina pectoris. For patients who experience considerable discomfort treatment is indicated. Definite foci of infection should be eliminated, but the routine exploration of sinuses, enucleation of tonsils and extraction of teeth is to be deprecated. Attention should be paid to the gastrointestinal tract. The food should be simple, well-masticated and not abundant. Drinking with meals is forbidden; tobacco and alcohol should be cut to a minimum. Where a nervous element predominates, sedative drugs are of value. Digitalis usually gives disappointing results but it may be tried. Quinidine sulphate in doses of five grains three times daily controls some cases.

Auricular Fibrillation. Auricular fibrillation, recognized for many centuries as "delirium cordis," is one of the commonest disorders of cardiac rhythm. It is usually associated with heart disease, particularly mitral stenosis. It frequently complicates hyperthyroidism and, if so, the arrhythmia is characteristically transient.

The pulse in auricular fibrillation shows an irregular irregularity. There is a variation, not only in rhythm, but also in volume. It is always advisable to record the apical rate together with the pulse, for the pulse may not give a positive indication of the ventricular rate since many of the smaller beats are not strong enough to open the aortic valves and thus the pulsations do not reach the radial pulse. Exercise increases the irregularity. Carotid sinus pressure has no effect on the irregularity.

Mackenzie first suggested the use of digitalis for auricular fibrillation. Many preparations of the drug are on the market, but for oral use the capsules or pills of powdered leaf, prepared by a reputable drug firm, are the best. Various methods of dosage have been advised, such as the large dose method, the small dose method and the body weight method. So far as I know, the advice of William Withering in his original article on foxglove in 1785 still holds today: "Let the medicine be continued until it either acts on the kidneys, the stomach, the pulse or the bowels; let it be stopped upon the first appearance of any one of these effects." Remember that it takes approximately 30 grains of the leaf for complete digitilization. A satisfactory way to distribute the dosage is to give three grains every four hours for six doses, then three grains three times daily for one day and follow this with a maintenance dose of one and one-half grains each day. In extremely urgent

cases, strophanthin may be given intravenously in an initial dose of 1/150 of a grain or ouabain in a dosage of 1/200 of a grain.

Quinidine is another drug that is extremely valuable in the treatment of auricular fibrillation. It is most useful where the fibrillation has been of short duration. Unlike digitalis, quinidine has the power of abolishing circus movement and restoring normal rhythm. With the patient in bed, a preliminary dose of three grains should be given to determine if there is any idiosyncrasy to the drug. If no toxic symptoms appear, carry on with six grains every four hours, day and night, except for the omission of one night dose during sleep. This dosage may be continued for seven to ten days. The pulse rate will increase, and then, in favorable cases, one day you feel the pulse and it is regular. Be on the lookout for toxic symptoms—marked tinnitus, deafness, nausea, vomiting, diarrhoea, a very rapid regular pulse. If any combination of these symptoms appears, the drug should be discontinued. In the early cases treated with quinidine, there were a number of fatalities due to embolism. This unfortunate complication occurred when the restoration of normal contraction in the auricles forced out thrombi from the auricular appendages into the general circulation. Today, with more careful selection of cases, this complication is less likely to arise. An ideal case for quinidine therapy is one in which the *fibrillation has been of short duration, in which congestive failure is absent, and there is no history of embolism and the heart is essentially normal in size.* In approximately 60 per cent of carefully selected cases, the normal rhythm will be restored and, once established, usually persists for weeks, months or years. It is, however, usually advisable to continue with a daily maintenance dose of quinidine.

A word should be said about auricular fibrillation associated with hyperthyroidism. Hyperthyroidism should always be suspected in cases of transient or paroxysmal fibrillation. It should be suspected as well, when, with complete digitilization, the ventricular rate fails to slow to an appreciable extent. In the great majority of cases of auricular fibrillation, digitalis in adequate dosage produces slowing of the ventricular rate to approximately a normal level. When the irregularity is due to thyrotoxicosis only occasionally can a normal rate be obtained. One should be on the lookout for the patient with masked or latent hyperthyroidism, for the two striking diagnostic criteria, exophthalmos and thyroid enlargement, may be absent. The recognition of this group is important, for there is no other type of heart disease in which recovery, even after extreme myocardial failure, is so satisfactory. Regarding therapy, there can only be one answer: careful preparation with Lugol's solution followed by a subtotal thyroidectomy is the ideal treatment. As Lahey states: "There are practically no thyrocardiacs in which the decompensation is due to a superimposed thyroidism that are not operable." Following surgery, many cases revert to a normal

rhythm. In those which do not, quinidine will almost always prove successful.

Auricular Flutter. Auricular flutter, like fibrillation, is usually associated with heart disease but may exist in a normal healthy individual with no evidence of myocardial damage. It is a disorder of auricular action characterized by regular but abnormal auricular contractions at a rapid rate, between 200 and 400 contractions per minute. The ventricular rate is usually one-half of the auricular rate because of the existence of a two to one auriculo-ventricular block. There may be a mixture of varying degrees of block which gives rise to an irregular pulse.

Auricular flutter is probably never present where the apical rate exceeds 200. Such a rate is more likely to be due to paroxysmal tachycardia. Flutter is probably present when the pulse rate ranges between 120 and 170, remains constant in all positions, is not influenced by rest or exercise and continues for days, weeks or months. A sudden doubling of the ventricular rate or the pulse rate increases the certainty of diagnosis. In most cases of flutter careful auscultation at the apex reveals a dominant rhythm. This rules out the possibility of auricular fibrillation. Carotid sinus pressure never terminates the paroxysm but produces a sudden significant slowing by increasing the grade of block and with release of pressure the original rate is resumed.

The patient with auricular flutter should be completely digitalized. In favourable cases, the flutter changes to fibrillation. If so, digitalis should be discontinued and in many instances the rhythm will revert to normal. Further treatment is unnecessary. If, in spite of digitalis, the flutter persists, but the ventricular rate assumes a normal figure, a maintenance dose of digitalis should be used. Quinidine may be given a trial. It should be prescribed as outlined for auricular fibrillation. In approximately 50 per cent of cases digitalis is successful; in a small percentage of cases, quinidine gives good results. There are, however, a number of cases in which all therapy fails to control either the auricular or ventricular rates. After a period of months or years the attacks may stop spontaneously.

Ventricular Fibrillation. Ventricular fibrillation, because of its extreme rarity except as a terminal condition, is of little clinical importance. A few cases have been reported, characterized clinically by temporary spells resembling "Stokes Adams" attacks. During the seizure auscultation reveals an absence of all heart sounds.

Auriculo-ventricular Block. Auriculo-ventricular block is due to depression of the function of conduction in the auriculo-ventricular bundle. This results in delay or obstruction to the excitation wave as it travels downward from auricle to ventricle. The condition may be temporary and functional, or permanent and organic. It may vary in degree from a slight delay in conduction or occasional dropped beats to a complete heart block in which there is absolute dissociation between the auricle and ventricle, the auriculo-ventricular node establishing an

independent ventricular rhythm, usually at a rate of 25 to 40 beats per minute.

An occasional dropped beat due to partial heart block may be distinguished from a ventricular premature beat that has failed to show itself in the radial pulse by auscultation. With complete heart block the pulse rate varies, but usually ranges between 25 and 40, the rhythm is regular, and evidence of heart disease is usually present. The blood pressure shows characteristically a high systolic with a low or normal diastolic reading. Exercise does not increase the pulse rate and neither rest nor vagal pressure slow it. Simultaneous auscultation at the apex and observation of the jugular vein reveal venous pulsations at a rate of 70 to 80 per minute and ventricular contractions at a slower rate. In many cases faint sounds due to auricular contraction occur in varying time relations to those resulting from ventricular contraction. If the auricular sounds coincide with the first or second heart sound, the latter are accentuated so that on auscultation a variation in the intensity and quality of the first or second heart sound may be noted. The combination of auricular fibrillation with complete heart block is distinguished by absence of the faint auricular sounds, for in auricular fibrillation the auricle does not contract, hence no sound is produced. Auscultation reveals only the slow rate with regular rhythm, no variation in the intensity of the heart sounds and no muffled sounds in the diastolic period.

Treatment should be directed at the probable etiological agent. The lesser grades of block, unless associated with myocardial insufficiency, require no particular therapy. With congestive failure, one should not hesitate to use digitalis. True, the drug may convert a partial to a complete heart block but, if the ventricular rate is sufficiently high to prevent syncopal attacks, clinical improvement is very often striking. The treatment of complete heart block is largely that of preventing "Stokes Adams" attacks. During a seizure, the subcutaneous injection of five to ten minims of a 1-1000 solution of epinephrine hydrochloride is of great value. For use over a prolonged period, ephedrine hydrochloride is the drug of choice, given by mouth in doses of one-half a grain three or four times daily. These drugs increase the activity of the idio-ventricular pacemaker and hence increase the heart rate. Barium chloride, thyroid extract and atropine, although at times useful, are usually less effective. Digitalis is indicated to combat congestive failure.

SUMMARY

The various tachycardias and cardiac arrhythmias have been discussed. An attempt has been made to show that many of the disturbances of heart rate and rhythm can be diagnosed at the bedside when meticulous care is taken. Appropriate therapeutic measures have been proposed.

John Hunter, Scientist and Philosopher

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IN order to appreciate and to comprehend John Hunter's labours and the stupendous and diversified contributions which he made to medicine, one must consider not only the man himself but the world in which he lived. Only by so doing can one form a true conception of the man.

HIS YOUTH

John Hunter was born in 1728. He came from an old Scottish family of Ayrshire, probably of Norman origin, whose history goes back to the thirteenth century. The Hunters of Long Calderwood were a younger branch of this family. Long Calderwood is an estate seven miles from Glasgow, and here in a room above the kitchen of the historic stone house on the night of February 13th, 1728, John Hunter, the last of ten children, was born. Of this large family, three alone were destined to live to maturity: Dorothea, who gave birth to the "immortal Joanna," one of Sir Walter Scott's closest friends; William, who became a famous London physician, and John.

John's father died when he was yet a boy, and he was left to be reared by a tender-hearted, oft-bereaved mother, who ruled the wilful lad with an all-too-gentle hand. In short, John was a spoiled child; he wasted his youth and, unrestrained, pursued until the age of twenty-one the whims of his childish and adolescent fancy. Throughout boyhood he was good at games and observant of nature, but he was deficient in self-control and idle, and would not attend school. He afterward said of himself: "When I was a boy I wanted to know all about the clouds and the grasses, and why the leaves changed colour in the autumn; I watched the ants, bees, birds, tadpoles, and caddisworms; I pestered people with questions about what nobody knew or cared anything about." He hated school books; nor did he see the good of learning even at Oxford in the few months that he wasted there long after boyhood was over. Of this episode he said: "They wanted to make an old woman of me, or that I should stuff Latin and Greek at the University; but these schemes I cracked like so many vermin as they came before me." Nature alone was the deity to which he made obeisance. Typical are his words to a pupil's parent: "Sir, follow me; I will show you the book your son has to study," and, taking him to the dissecting room and showing him the bodies, he said: "These are the books your son will learn under my direction, the others are fit for little." Though Hunter disdained all book knowledge and opportunities for education, this very thing was later to prove a severe handicap to him, because it, more than

any other factor, is doubtless the reason for the frequent obscurity of his writings.

Hunter was a man of great courage, and this trait can best be illustrated by referring to an incident which occurred in Scotland when he was twelve years old. The Scots were a superstitious people, and they were imbued with the clerical teaching that Satan frequently appeared in corporeal substance and seized persons and carried them away in the air. One night while Hunter was chatting in a neighbor's cottage, a terrible face, resembling that of the Devil, appeared at the door. The cottagers, one woman and two men, were motionless, petrified with fear; not so John, who, though he afterwards confessed he was by no means sure that it was not the Devil, snatched up the fire tongs and, attacking the spectre, made it roar with pain and run out of the house.

Little good can be said of the first twenty-one years of John Hunter's life, for these years were spent in idleness and dissipation. His brother William, ten years his senior, had gone to London and established for himself a reputation as a surgeon. But John eventually tired of his idle ways and wrote to his brother, asking permission to go to London and assist him in his anatomical researches. To this letter he received a very kind reply, and so we find him, a short, stocky, broad-shouldered, red-haired Scot, eyes flashing a restless and indomitable energy, making the trip to London, fortune and fame.

EARLY YEARS IN LONDON

Arriving in London in 1748, after a fourteen-day journey on horseback, he immediately started dissecting. The quality of his work from the outset won the approval of his brother, who forecast for him a successful career as an anatomist. Anatomy from the first held John's interest, and the ensuing eleven years of his life were spent almost solely in the dissecting room. The unhealthy atmosphere of the anatomical laboratory of that time had a deleterious effect on his health, and short respites from his labours were necessary, one being a visit to the old house at Long Calderwood in 1752 and another a short stay at Oxford in 1755.

In the summer of 1759, Hunter received very definite warning that his assiduous application to the study of anatomy was seriously affecting his health. This came in the form of an attack of pneumonia and, considering that seven of his family had already died of lung affections, most of them certainly of phthisis, the warning was too definite to be ignored and a prolonged change of occupation was decided upon. He secured a commission in the army and spent the years 1760-62 as a surgeon in the expeditions to Belleisle and Portugal. Characteristically, here as elsewhere, he was always at odds with his colleagues, partly because he was always attempting to try a new method of treatment which happened to suggest itself. Of his superiors he wrote: "My fellow creatures of the hospital are a damn'd disagreeable set. The two

heads are as unfit for their employment as the Devil was to reign in Heaven."

In the two years which he spent as army surgeon, he produced the last part of his great work, "The Treatise on Blood Inflammation and Gunshot Wounds." He made observations whenever opportunity offered, for already his inquisitive mind and capacity for work would not allow him rest for a moment.

Returning from the Peninsular War, Hunter was faced with the problem of establishing his reputation. He was already thirty-five; he did not have the art of attracting patients and, moreover, his passion for scientific research interfered with his success as a surgeon. To the people around Golden Square, he was a zealous student of the human body who might or might not restore one's health but who would certainly wish to anatomize one if he failed. On his marriage to Miss Ann Home, his rapidly increasing fame as a surgeon and teacher of anatomy in London, his purchase of a large country establishment, Earl's Court, which became a veritable naturalist's paradise where he kept everything from the fresh water mussel to the timorous zebra, I shall not dwell here except to state that the fact that Hunter married Miss Home, who was a lady of the highest rank and from the best society, should still forever the calumnious words of Jesse Foot who described him as a man, debased and debauched, seeking and enjoying the society of the low-minded.

HIS PHILOSOPHY

In order that one may understand the thoughts and writings of Hunter, I shall make brief note of his method of approaching his problems. As is well known, there are two methods of reasoning, the inductive and the deductive. The inductive method begins with facts and works up to general principles; the deductive begins with general propositions and reasons from them to individual cases. The philosophy of antiquity was essentially deductive, but just before the advent of John Hunter, Francis Bacon had introduced into England the new inductive method. Bacon did not discover this inductive method of reasoning but it was he who directed men from ecclesiastical and verbal disputations to the discovery of truth by observation and experiment. In England, the gradual growth of enlightened skepticism and inquiry, which in religion conduced to tolerance, in politics to freedom and in physics to natural science, came to the front in the sixteenth century and was confirmed by the Revolution of 1688.

Hunter arrived in an England which was deeply imbued with the Baconian spirit. Scotland, also, was for the first time in history producing a class of enterprising and thinking men whose aims were essentially secular—and this at a time when the country was the most superstitious and priest-ridden in the world. Centuries of ecclesiastical supremacy had influenced the nation in favour of the theological method of reasoning, and in such an atmosphere inductive philosophy was prac-

tically impossible. So we find all the great Scottish thinkers of this period using the deductive method of reasoning. It has been abundantly proved that knowledge is never widely disseminated among the peoples of a nation where deductive reasoning is used. The deductive process, dealing with abstract ideas, appeals to the thinking faculty and not to the senses and, as ideas are more difficult to grasp than facts and, as there are more good observers than great thinkers, induction influences the popular mind much more than deduction.

A study of Hunter's works shows that he combined to an exceptional degree the two philosophical methods. Hunter was essentially a thinker rather than a scholar, and yet he was an experimental philosopher rather than a metaphysician. He saw that for a complete system of knowledge deduction and induction were supplementary to each other, and that when all the intellectual resources of man were fully developed, then these methods would no longer be regarded as hostile to one another. Hunter employed the deductive method largely; he reasoned downward from premises and hypotheses which he deliberately invented and in so doing arrived at conclusions. Although these were often unproved, inaccurate or only approximately correct, it is astonishing how many of his speculations in physiology and pathology, made at a time when microscopy and clinical science were in a backward state, have been confirmed. Thus did his genius often outstrip facts and anticipate discoveries. Hunter's use of inductive reasoning is illustrated by his scheme of classification, by his patient and careful anatomizing of so many hundreds of different species of animals, and by his untiring investigations of diverse structures and organs. It was chiefly by these methods that he concentrated the scattered facts of comparative anatomy and thereby advanced physiological science. Many arguments and inferences from analogy occur in his writings; some amounted to the most perfect induction, others led him into error.

Much of his pathology was based also on the inductive process. Great as a physiologist, he was still greater as a pathologist, in which science, considering what it had been before his time, he was without a rival. It was here especially that his depth of insight, his profundity of thought, and his comprehensiveness of mind marked him as a genius. His was a pathology not only of man but of the whole animal and vegetable kingdoms. His outlook was the more inclusive when we consider that it embraced not only the whole of the organic world, but the deviations from the typical of the inorganic also.

The reason Hunter adopted both these methods of reasoning was probably not because he came into intimate contact with the two distinct types, so much as because of the natural scope and bent of his mind and the nature of the subject to which he devoted his life. Induction, of course, is largely the method required for the profession he chose, yet on the other hand, being a great thinker, he naturally inclined to the deductive method. It was not, however, as a logician but as an observer

and experimenter that Hunter excelled; it was not the beauty of his logic but the industry with which he collected facts, and the ability and honesty with which he reasoned from them, which made him great. If it is true that the obscurity which was often evident in Hunter's works, was due to the conflict of these two methods of reasoning, the perplexity probably arose from the very comprehensiveness of his mind and the vastness of its conceptions.

HUNTER THE SCIENTIST

His keen observation and capacity for work are shown to best advantage in his work as a biologist, physiologist, and museum collector. From his period as army surgeon we have, perhaps, his first recorded physiological experiments. Quoting his own words, we have a good illustration of the simplicity of his method:

"At Belleisle, in the beginning of the winter of 1761-62, I conveyed worms and pieces of meat down the throats of lizards, when they were going into winter quarters, keeping them afterwards in a cool place. On opening them at different periods, I always found the substances which I had introduced, entire, and free from any alteration: sometimes they were in the stomach; at other times they had passed into the intestine; and some of the lizards that were preserved alive, voided them towards the spring, with but very little alteration in their structure."

"In the year 1762, when I was in Portugal, I observed in a nobleman's garden, near Lisbon, a small fish-pond full of different kinds of fish. The bottom was level with the ground, the pond having been made by forming a bank all around, and had a shrubbery close to it. Whilst I lay on the bank observing the fish swimming about, I desired a gentleman who was with me to take a loaded gun and fire it from behind the shrubs. The moment the report was made, the fish seemed to be all of one mind, for they vanished instantaneously, raising a cloud of mud from the bottom."

The overwhelming volume of his zoötomical work, perhaps, accounts for the imperfect recognition of his botanical researches. The vegetable kingdom claimed a great share of his attention. He recognized the relationship between inorganic and organic matter, and rather remarkably restricted to the vegetable kingdom the power of immediately converting common (inorganic) matter into its own kind, and placed plants as an intermediate link between inorganic matter and animals. He drew analogies between many of the vital functions of plants and animals; so, he compared the flow of sap in trees to circulation in animals. Even the most minute detail failed to escape him; he noticed, for instance, that certain twining plants encircle their support in a constant direction.

Here is a characteristic example of the way he worked. Referring to his observations on the plant *Mimosa pudica*, he writes: "In order to have the greater part of the day before me, I began my experiments at eight in the morning whilst the leaves were in full expansion, and

I continued them till four in the afternoon as longer would not have been just, for they begin to collapse of themselves between five and six o'clock."

One wonders at the diversity of his ambition and marvels that the very magnitude of his work did not obscure the pursuance of any one purpose. So he was at one and the same time interested in the anatomy of the bee and its hiving instincts, heat in plants, metabolism in hibernating animals, and the classification of a new species of animals, all the while that a large London practice was commanding the greater share of his time. He was able to accomplish all this only by stealing the necessary time from his working hours and by snatching it from his sleep.

To the field of zoological and physiological science he made a vast contribution. His devotion to physiology in particular had its root in a conviction of the necessity of this branch of instruction for the intelligent practice of surgery, yet this was made a reproach by surgical contemporaries who called him a theorist and not a practical surgeon. He made the blood and the vascular system the subject of intensive study; he recognized that the coagulability of the blood was influenced by temperature; in fact, the final outcome of all his experiments and observations on the blood was a view of coagulation which harmonizes closely with that of the present day. This can best be stated in his own words: "The fluid state of the blood is connected with the living vessels, which are its natural situation; and with motion; and where there is a full power of life, the vessels are capable of keeping the blood in a fluid state." He determined that there were two layers of tissue in the arterial wall, an inner muscular and a protecting, outer fibrous layer. He recognized the principle of collateral circulation, correctly interpreted it, and was encouraged to operate for aneurysm.

Possibly no great truth, apart from Harvey's discovery of the circulation of the blood, has been so completely demonstrated as Hunter's law of bone absorption and bone modelling, and a study of his work on bone reveals how far he was in advance of his time. It was he who fed his animals on madder until their bones were red with it, and it was he who conceived the idea of osteoblasts and osteoclasts in bone repair and natural growth. With such illustrations of the lasting truths which Hunter discovered, we are struck with wonder that his true greatness is so little appreciated. Perhaps the reason why so many of his discoveries are not generally known or recognized is because he did not use the words we now employ to describe these phenomena, or because he lacked clarity of expression, or because his observations so pack the printed page that their study requires the closest observation.

The discovery of micro-örganisms, phagocytes, and toxins did not put Hunter's work out of date; instead his "morbid poisons" became "micro-örganisms" and the manifestations he called "sympathies" were translated into "toxic effects." Whatever the underlying mechanism, the phenomena he observed and described were manifestations of living

matter reacting to disease, and they will remain and will be recognized as long as life exists. It is interesting to note how nearly Hunter approached the truth in explaining the great principles of disease in spite of his ignorance of micro-örganisms: He said, "The most simple idea I can form of an animal being capable of disease is that every animal is endued with a power of action and a susceptibility of impression, which impression forms a disposition, which disposition may produce action, which action becomes the immediate sign of the disease; all of which will be according to the nature of the impression, and of the part impressed." Interpreting this, in the light of present knowledge, we learn how far Hunter had progressed in surgical pathology. His "power of action" we speak of now as the "predisposition to" the disease, or the "diathesis"; the "susceptibility of impression" is the "infective organism." The "disposition" is the "exciting cause"; and the "action" is the "manifestation of the disease by signs and symptoms." He stated: "A true specific disease is one that probably cannot arise but from one cause, and which probably always belongs to morbid poisons; so scrofula is one of those diseases which is supposed to be hereditary, but it is only a readiness to fall into the peculiar action when properly irritated that is hereditary, and when such a cause does not exist we have no scrofula." Surely here the key alone was lacking, a key which was forged seventy years later by Lister and Pasteur.

Of his museum, his all but consuming passion, to the collection of which he gave his time and fortune unstintingly, we can make bare mention. That he spent no less than £70,000 on this alone and died scarcely able to pay his debts; that he lavished on science the income he made at the risk of his life by the hard work of practice; and that even in ill-health and under the shadow of death he never rested from his incessant task of collection, dissection, observation and experiment is tribute enough. His personal collection numbered over 14,000 specimens, with ten volumes of manuscript, drawings and notes, and he left record of having dissected with his own hand over 500 species of animals. Was ever man a more prodigious worker? Studying Hunter's collections one cannot fail to be impressed with the master's work, for the list of preparations is not merely a bald presentation of facts, but each preparation unfolds a tale, each conveys a lesson, each is a link in a chain.

THE MAN HIMSELF

Now for a glimpse of the man himself and his handicaps. His limitations were great. Hampered by a defective education, he was often at a loss to express himself; his metaphors were often strained or wholly false and he was confessedly ignorant of the work of his colleagues and contemporaries. There was no chemistry in his day, no physics, no knowledge of animal cells, and hardly a theory of fermentation to account for disease. He was obliged to stumble on as best he could, for he was half a century before his time; but, as I have shown, in spite of this he very frequently arrived almost at the truth, and his

writings are full of the most astounding presages of knowledge to come, some of which still await their accomplishment.

Perhaps his most severe handicap was ill-health. Practically the entire latter twenty years of his life were darkened by the shadow of death and his waking hours were maddened by pain. The reason for this can be traced to a certain Friday, in May 1767, when he inoculated himself with pus from a gonococcal lesion in an experiment to determine whether the poison of gonorrhoea was identical with that producing syphilis. He satisfied himself that they were identical and obscured the literature for many generations by his error. In the light of present knowledge, we know that he inoculated himself with three organisms, the gonococcus, the Treponema pallidum, and Ducrey's bacillus; how efficacious his later antisyphilitic treatment was is indicated by his subsequent illness. He may, therefore, be considered as one of the martyrs to science, although I feel that he was not justified in his martydrdom, because the consequences of his experiment were visited upon himself and his children, and all surgery suffered by the wanton shortening of his life.

Hunter suffered from syphilitic endarteritis which manifested itself from 1773 until his death in 1793, during the time when he made his vast and lasting contributions to science. That the higher faculties of his mind were spared by the disease and only the lesser cerebral symptoms were produced, seems significant. It apparently never occurred to him to associate any part of his ill-health with his experiment upon himself, for he expressly says: "It would appear that some parts of the body are much less susceptible of the lues venerea than others, and not only so, but many parts as far as we know are not susceptible of it at all, for we have not yet seen every part of the body affected; we have not seen the brain affected."

Besides cerebral symptoms, he was subject to severe, paralyzing anginal manifestations and, as these became more easily provoked, they became a greater handicap to him until, finally, the slightest physical exertion, such as rolling over in bed, any agitation of mind, or even a surgical operation attended with any nicety, was apt to precipitate an agonizing attack. Hunter always had an ungovernable temper, and it was this which proved his undoing, for it was an anginal attack precipitated by a fit of rage, brought on by dissension with his surgical colleagues, that caused his sudden death in 1793. There is small wonder that men marvel at the accomplishments of the man and the unquenchable fire of his spirit in the face of such odds.

The output of Hunter's working life was fivefold—literary, surgical, anatomical, philosophical, and experimental; but the summation of these factors does not give the whole result of his work. He brought surgery into closer touch with science. Contrasted with Ambrose Paré, a surgeon, in some ways like Hunter, shrewd, observant, far in advance

of his time, the achievements of the latter along side those of Hunter are as child's play.

Hunter was like Vesalius; he made his name immortal by the labour of his own hands outside the sphere of surgery. It is when we compare what he did and thought with the deeds and thoughts of the medical men with whom he has been compared, that we are forced to place John Hunter in the same unique position in medicine as that assigned to Shakespeare in literature.

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BREATHING OF AMNIOTIC FLUID AS A NORMAL FUNCTION OF FETAL RESPIRATION

By F. SNYDER AND M. ROSENFELD

Proc. Soc. Exper. Biol. and Med.; 36:45, 1937

India ink was injected into the amniotic sac of rabbits. Breathing was suppressed in the control rabbit fetuses by injecting pentobarbitol sodium into the amniotic sac with the india ink. In the experimental rabbit fetuses, carbon particles were found in the alveoli of the lungs, thus proving that amniotic fluid is a normal content of fetal pulmonary alveoli.

—B. BEAL, '39.

SULPHANILAMIDE TREATMENT OF BUBO WITH

By A. HUTCHINSON

Lancet; 1:1047, 1938

In a series of 35 consecutive proven cases of bubo, 12 cases were treated with local applications, 12 with Dmelcos vaccine and 11 with sulphanilamide in doses of one gramme every four hours, with a maximum dosage of 138 grammes. The average stay in hospital in the cases treated with local applications was 46.2 days, in those treated with vaccine 46.7 days, while in the cases treated with sulphanilamide the average period of hospitalization was only 15.5 days.

—R. MCCALLUM, '39.

A Review of the Literature on the Treatment of Cancer of the Breast

By C. ROBERT KEMP, B.A., '38

IN a discussion of the treatment of breast cancer, the important methods of which are surgical and radiological or a combination of the two, it would be wise first to review the anatomy and the lymph drainage of the breast.

Anatomy

The breast is formed from modified sebaceous glands and, as such, lies in the superficial fascia. It is fixed to the skin at the nipple and at numerous other points by fibrous strands, the suspensory ligaments of Astley Cooper. Each mamma consists of from 12 to 20 lobes arranged in a radial manner as sectors of a circle. Each lobe is complete in itself with its alveoli, collecting tubules, and main duct, which dilates to form the ampulla just before it opens on the surface of the nipple. At various periods in a woman's life, the actual composition of the breast is different. At puberty, there is a rapid development of the acini and a deposition of fat between the growing lobes. During pregnancy, many new alveoli are formed and the proliferation is so rapid that these alveoli consist of solid cords of cells, until parturition initiates lactation. At the menopause, there is involution of the mamma, when the fatty tissue atrophies and the fibrous tissue, increasing in amount, contracts and causes gradual atrophy or even complete disappearance of the alveoli.

In a normal adult female, the breast extends vertically from the lower border of the second rib to the angle of the sixth costal cartilage and transversely from the edge of the sternum at the level of the fourth rib to the mid-axillary line at the level of the fifth rib. There is usually a tongue-shaped projection, known as the axillary tail of Spence, which extends up to the level of the third rib in the axilla, where it is in direct contact with the anterior axillary lymph glands. It should be noted that the axillary tail passes under the deep fascia and thus is not like the rest of the breast tissue, which is superficial to the deep fascia. The upper and medial two-thirds of the mamma lies on the pectoralis major muscle. The lower and lateral portion lies mainly on the serratus anterior muscle. Part of the tissue of the lower medial quadrant of the gland lies on the aponeurosis of the external oblique muscle which separates it from the rectus abdominis. The outlying breast tissue extends as a thin marginal fringe in the subcutaneous fat considerably beyond the limits of the breast prominence.

The arterial blood supply is from three sets of vessels: (1) the lateral thoracic artery; (2) perforating cutaneous branches of the internal mammary artery, to the second, third and fourth interspaces;

(3) lateral branches of the second, third and fourth intercostal arteries.

The venous drainage is similar to the lymphatic drainage in that there is a plexus beneath the areola from which large vessels pass to the axillary and internal mammary veins.

Lymphatic Drainage

The breast is richly supplied with lymphatic vessels. Each lobule has its own system of vessels which are in close relation to the acini. The lymphatic vessels from the central part of the gland pass along the ducts to a subareolar plexus, the plexus of Sappey, which also receives the lymphatics from the skin over the central part of the mamma, and from the areola and nipple. Many of the lymphatic vessels pass deeply and communicate with the pectoral lymphatic plexus, which lies on the pectoral fascia just beneath the gland. The pectoral lymphatic plexus is not a definite single plexus but is rather a part of the deep fascial lymphatic plexus whose anastomosing branches form a complete network over the whole body. Large lymphatic trunks connect the subareolar and pectoral plexi with the inferior lymph glands upon the medial wall of the axilla. One large trunk from the upper part of the mamma, however, arises on the posterior aspect of the mamma, pierces the pectoralis major muscle and terminates in the subclavicular lymph glands, without first passing into the axillary group. Thus, these may be involved secondarily with malignancy before the axillary group, and, because of their sheltered position, may escape removal at operation.

Another route of drainage is along the vessels which accompany the branches of the internal mammary vein. These lymphatics perforate the chest wall in the second, third and fourth intercostal spaces at the edge of the sternum, and terminate in a group of glands, the parasternal or anterior mediastinal glands. It is noteworthy that in this region the pleura is very thin. There is a communicating trunk from the upper parasternal gland to the supraclavicular glands.

The lymphatic connection with the other breast is through the medium of fine vessels of the fascial plexus. Thus, cancer can only spread to the opposite breast in a late stage after permeation has crossed the mid-line.

From the lower medial quadrant of the breast there are some lymphatics which pass downwards to communicate with the subperitoneal lymphatic plexus.

Sampson Handley does not believe in the widespread communication of a skin plexus. He states, "The only communication between adjoining lymphatic areas of the skin appears to be by way of the fascial lymphatic plexus." He explains the secondary nodules often found in the skin as resulting from a retrograde growth of tumour cells up a terminal lymphatic from the fascial plexus to the skin.

Other authors, Lee McGregor, for example, describe the lymphatic system of the breast under the two headings: (1) Lymphatics of the

Overlying Skin, and (2) Lymphatics of the Parenchyma of the Breast. The recent work of J. H. Gray at St. Bartholomew's Hospital is very illuminating. By the use of thorotrast and barium, the lymphatics were made visible and their course traced out more accurately than ever before and it was shown that there is no lymphatic plexus in the deep fascial layers. It was found that the lymphatics lie in the gland substance and on its surface. This fits in with the system of lymphatics as given by McGregor.

In summarizing the possible routes of spread and the sites to which cancer may metastasize from the breast by the lymphatics, we find that it may pass,

(1) To the axillary glands via trunks from the fascial plexus,
(2) To the subclavicular glands from the fascial plexus,
(3) To the parasternal glands via the perforating lymphatics,
(4) To the supraclavicular glands from the upper parasternal gland,
(5) To the opposite breast by permeation through small communicating vessels of the fascial plexus,
(6) To the subperitoneal lymphatic plexus through the upper thin part of the linea alba,
(7) To the inguinal lymph glands via small communicating branches of the fascial plexus.

The above list includes only the immediate secondary sites. From these, extension may proceed by lymphatic chains, by the blood stream or by direct growth, to the cervical glands, brain, lung, bones, peritoneum, liver, pouch of Douglas, and other sites.

TREATMENT

In reading the current literature on the treatment of breast cancer, one is astonished at the great variability of opinion as to the methods and their respective merits and results. Diametrically opposite opinions are expressed by great men. As yet, the results are tragically poor, using any method.

The methods are multiple as they are in any disease for which there is no specific cure. However, as yet, surgery and radiology, alone or in combination, have given the most satisfactory results. I will attempt to give a brief survey of some of the current opinions on the various methods as used today.

Surgery. Cancer of the breast is one of the most ancient of the recognized diseases. Almost as old as the disease is its surgical removal, although at various stages treatment by plasters, caustics and counter-irritants has predominated.

Sigerist states, "The history of the therapy of cancer is very dull. The principles we are following today, namely the elimination of the tumour as radically as possible, were discovered in far remote antiquity. Our operative methods are much more efficient than theirs were, and besides the knife, we have X-rays and radium to destroy the tumour cells, but we have not found any new principles yet."

Celsus, realizing the great futility of any kind of treatment, wrote, "Some physicians used caustic remedies. Some cauterized and others operated with the knife. The remedies, however, never did any good to anybody. All we can do is to watch and see what will happen."

Leonides, an Alexandrian surgeon of the second century, A.D., apparently had a method of operating on cancer of the breast. He operated only when the tumour was not too far advanced. He excised the breast with a scalpel, making his incision through sound tissue and then cauterized the wound to arrest haemorrhage and destroy any remaining cancerous tissue.

Haagensen describes Henri Francois Le Dran (1685-1770) as "the most enlightened cancer surgeon of the eighteenth century." He states, "For the first time the humoral conception of the disease (as postulated by Galen) was entirely discarded. Le Dran regarded cancer as a local disease in its early stage. He knew that it spread via the lymphatics to the regional nodes and thence into the general circulation. He described with clarity the path of metastasis in breast carcinoma, including involvement of the lungs. He realized that the only hope of cure lay in early operation. He dissected out enlarged axillary nodes in breast carcinoma, at the same time remarking that when nodes were found to be involved the hope of cure was slight." . . . "All this was a tremendous advance over the previous knowledge of cancer and Le Dran deserves to be recognized as one of the greatest figures in the evolution of our knowledge of the disease."

The nineteenth century saw many advances in the field of surgery of the breast. Astley Cooper, in 1840, wrote a very excellent paper on the anatomy of the breast, in which he described the lymphatic channels as he found them by dissection after mercury injection. He believed in the removal of the axillary glands as part of the surgical treatment. In the middle of the century, the advent of anaesthesia made deeper and more thorough dissection of involved glands possible. In 1867, Charles Moore formulated the general principles upon which the modern surgical attack is based. He advocated the complete removal of the adjoining skin, lymphatics, fat, pectoral muscle and axillary glands, with the whole dissection being done in one piece, without cutting into or seeing the tumour itself. Halsted first described his method of radical mastectomy in 1891. It is described as the greatest contribution ever made to the treatment of breast cancer. The method has passed through many minor transitions, but basically it is the same. In "Christopher's Surgery" over a score of modifications of the incision used are explained and illustrated.

The Halsted operation which is the basis for most of the modern methods was first used about 1890. Halsted in a letter, written in 1922, says, "You ask me to say something of my share in the development of the operation for cancer of the breast. . . . I advised and practised the removal of the entire muscle (pectoralis major) leaving in most instances the upper or subclavicular bundles; I divided the pector-

alis minor to further facilitate the cleaning of the axilla. . . . I insisted that all the tissue be removed in one piece and upon the meticulous cleaning of the axilla and its aestuaries (subclavicular and supraclavicular fossae). I warned against the danger of excising pieces of malignant tumour for microscopic examination unless the operation followed immediately. . . ."

Halsted advised an extensive removal of the skin over the tumour and made no attempt to close the wound. He then covered the large exposed area of the chest wall with Thiersch skin grafts and thus ensured healing of the wound without tension.

Sampson Handley, however, does not believe that so large a piece of skin need be removed, but favours a great deal of undercutting with wide removal of subcutaneous tissue and fascia. He states that the purpose of the operation is "to remove intact the permeated area of the lymph-vascular system which surrounds the primary growth, in one piece with the lymphatic glands which may have been embolically invaded along the trunk lymphatics of the permeated area."

Whether the contents of the axilla or the breast proper are removed first appears to be only a matter of choice with the surgeon, but all emphasize that the involved tissue should be removed in one piece. A thorough cleaning of all tissue from the axilla, except the blood vessels and nerves, is essential.

The use of a "hot loop" knife, cautery, or radio knife has been advocated by J. Anderson of Dundee and others. Its advantages are that it prevents an excessive loss of blood, it seals over the lymphatic vessels and prevents the invasion of tumour cells and it sterilizes and kills tumour cells for some distance on each side of its path. There is also less postoperative pain and very much less shock. The disadvantages are that it may not be used where an inflammable anaesthetic is being used, it must be carefully adjusted so as not to devitalize an area of skin when it is used in undercutting and so cause a slough, and there is a period of lowered resistance of about 7 to 10 days postoperatively in which the wound is more susceptible to infection.

Dean Lewis expresses the opinion of many surgeons in his belief that a radical operation should be performed and no compromise made regardless of the apparent size and extent of the tumour. Harrington also favours radical primary removal. He states, "The poorest surgical results in carcinoma of the breast are obtained after the secondary radical amputation after a primary partial removal of the tumour." He does not use a standard skin incision, but plans the incision in each case so as to remove the greatest amount of skin over the diseased portion and leave the least deformity and restriction of movement.

Eggers says, "An attempt has been made to show on the basis of accurate figures that radical surgical procedures offer the best chance for cure." He believes that the use of irradiation is as yet far too complicated for general use alone and that the possible complications

of irradiation would discourage the use of it as a routine procedure. In combination with surgery he thinks that it tends to make the surgeon careless and incomplete in the removal.

The advisability of simple removal of the breast as opposed to the radical operation is not generally accepted. However, E. J. Grace states, "I feel that the cure of cancer of the breast is theoretically best served by radical mastectomy; however, when we evaluate the end results, we are immediately compelled to stop and debate whether this theory of radical mastectomy is logical in view of our present results and knowledge concerning cancer." He advocates simply removing the mamma with a cautery and searing over the surface of the pectoralis muscle. In a series of 40 cases, treated in this way, he found the five-year end results to be very similar to those obtained where a radical operation was performed.

Irradiation. The use of irradiation in cancer therapy is as yet in its infancy. In December, 1895, Roentgen reported new rays which he called "X-rays" and, two months later, Becquerel reported the radio-activity of uranium. In 1898, Pierre and Marie Curie isolated radium. Sjogren, in 1899, successfully treated an epithelioma of the cheek with X-rays and, in 1903, Goldberg and London used radium for cancer treatment. Robert Abbe was the pioneer in the irradiation therapy of cancer in America. He treated inoperable breast cancer with radium and noted regressive changes.

The value of radiotherapy in inoperable cancer of the breast is generally accepted. Much may be done by this method to relieve the distressing symptoms and to impede the progress of the neoplasm. Metastasis may be temporarily controlled by irradiation. On operable cancers the relative value is still very doubtful. Recently its use on some early operable cases gave very good results, but months after the irradiation, even with marked diminution in the size of the tumour, a biopsy revealed the presence of cancer cells and mitoses.

Irradiation may be carried out in two ways: First, by the use of high-voltage X-rays (Coutard method) and, secondly, by the use of radium or its derivatives.

Coutard says, "Roentgenotherapy of cancer of the breast is, and probably will remain, one of the most difficult radiation problems for a long time." Realizing that large doses are essential for the clinical arrest of the cancer and to prevent the concomitant injury to adjacent normal tissue he applies the principle of fractionating and protracting the total dosage over a longer period. He believes that certain very high grade malignant cancers spread very rapidly and more extensively than may be shown clinically. This type of cancer is especially radio-sensitive and is probably best treated by radiotherapy, which will give a marked clinical improvement. These radiosensitive tumours are the ones which have little fibrous tissue and do not adhere to adjacent structures.

Keynes of London, England, writes very enthusiastically on the

use of radium in the treatment of breast cancer. Concerning the new anatomical findings of Gray, he says, "If Gray's observations are correct it will be necessary to revise our conception of the spread of cancer, and then perhaps the idea of conservative treatment of cancer of the breast may become more acceptable to us." He advocates local removal of tumour or breast, if the tumour is large, and interstitial radiation with radium needles. He doesn't believe that the "mutilation of a radical removal" is justified. Dissection of the axilla is absolutely contra-indicated in his opinion. He claims a definitely better survival rate than is obtained by the use of surgery.

Moreover, McKittrick of Boston, after using Keynes' method of interstitial irradiation, states, "Interstitial irradiation is an efficient and practical method of irradiating a breast cancer." He believes that it is better than deep irradiation by X-ray, but that, in a primary operable case, it is less desirable than surgery. He says, "It cannot be depended upon to protect the axilla against metastatic invasion."

Combined Use of Irradiation and Surgery. This is indeed a very moot question. Some of the surgeons are strongly for the use of irradiation along with surgery, some are doubtful as to its value but use it with hope and others are definitely against its use.

Irradiation may be used before or after the operation which may be a simple removal or a radical mastectomy. Aside from the irradiation of the breast, many men agree with Lens who says, "Irradiation of the ovaries is very valuable to sterilize and prevent a possible pregnancy which would rile up the metastases." An artificial menopause should be produced in young women with breast cancer as there is believed to be a definite association between it and the ovarian hormone.

Moore of Texas, favors pre-operative radiation by X-ray, then a radical operation in two or three weeks followed by implantation of radium and a course of postoperative irradiation by X-ray.

Trout says, "Preoperative irradiation is probably the most important contribution of radiologists to the treatment of cancer of the breast and is now generally regarded as being even more important than post-operative treatment." Even if the use of irradiation only prevents the local skin recurrences, its use is justified.

Lens believes that both pre- and postoperative irradiation should be used.

Adair and Stewart, in a report, state, "In the light of the studies here reported, it is our impression that the five-year cures will be definitely increased by the use of preoperative irradiation, and that it should be employed in all cases of cancer of breast complicated by pregnancy, in all cases with bulky axillary disease and in young women."

Cohn, of Baltimore, says, "I feel very strongly that there should be no restriction of the complete operation because of preoperative irradiation. If such limited statistics indicate anything, it is interesting to note that there is apparently no evidence that preoperative irradiation

prolongs the duration of life in those persons who are to die of the disease."

Harrington is definitely against radiation as shown by his statement that "Preoperative radiation causes an inflammatory reaction favouring dissemination. Postoperative radiation does not lengthen life nor improve the final result from operation." His results show that those patients who didn't receive radiation lived longer than those who did. Only in cases of the highest grade of malignancy does he advise radiation at all.

Greenough in his cases could find no beneficial results from the use of irradiation with operation. He believes the best treatment is radical surgery alone.

Many other names might be cited who are in favour of the combined use of surgery and irradiation and many others who think it valueless and even harmful.

CONCLUSION

The further one searches in the current literature, which abounds with work on the treatment of cancer of the breast, the more bewildered one becomes. Even our foundation of surgery and anatomy seems to be none too secure, as shown by recent findings. Because of the great multiplicity of factors, results have been published on one page of a journal which are contradicted by others published on the next page.

In all, the results are none too good, although there is quite a degree of optimism now, as the public are becoming more "cancer conscious" and are seeking aid earlier.

Many are the methods which are being employed in an attempt to cure this dread disease. As yet there is no specific treatment. It must be left up to the opinion of the doctor treating the case as to which are the best methods to employ in an attempt to eradicate the cancer or give relief to the patient.

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NOTE: References 1 and 19 were taken from the Memorial Hospital Fiftieth Anniversary Symposium, 1884-1934.

THE CLINICAL SIGNIFICANCE OF THE VENOUS PRESSURE

By J. CRAWFORD

Med. Times; 66:166, 1938

The information gained by the simple clinical study of the venous pressure in cardiac cases is of at least as much value as that obtained from the more routine estimation of arterial pressure. The fundamental physiological causes of circulatory disturbances, a differentiation of their types and the evils accruing from their altered mechanisms are discussed. Those types in which a rise of venous pressure is significant are described. A rise in venous pressure in both the pulmonary and peripheral circulation is seen in a large percentage of cases, but they frequently occur separately, hence the physical signs of congestion of both circulations are separately considered. The cardinal sign of pulmonary venous congestion is basal rales, and distention of the neck veins is the early sign indicative of peripheral venous congestion. Observation of the degree of distention of the neck veins, with the patient in the vertical position, affords an accurate estimation of the venous pressure, and is utilized in the Lewis method, recommended for clinical use. It is emphasized that elevation of the venous pressure in any cardiac, renal, or acute infectious condition is a demonstration of the onset of cardiac failure. Venesection, with withdrawal of about 500 cc. of blood is recommended in cases of high venous pressure, for it reduces the excessive cardiac load, permitting recuperation of the heart to a degree facilitating adequate function and normal circulation. If no benefit results, a permanently damaged heart is indicated.

—K. SYMINGTON, '40.

GASTRIC ACIDITY AFTER GASTRO-ENTEROSTOMY

By C. HOLMAN AND W. SANDUSKY

Am. J. Med. Sc.; 195:220, 1938

The gastric acidity was investigated in 75 patients suffering from peptic ulcer, before and after a posterior gastro-enterostomy was performed. It was found that in 92 per cent of the cases the gastric acidity was not altered, in eight per cent the acidity was diminished to below normal, but in only one patient did a complete anacidity result. The author concludes that an alteration in gastric acidity is not responsible for the beneficial effects sometimes derived from operation, and that the prognosis cannot be based upon the post-operative gastric acidity.

—N. BOYD, '39.

APPENDICEAL COLIC

By D. ROBERTSON

Can. Med. Assn. J.; 38:443, 1938

The physiological functions of the vermiform appendix are in general similar to those of the large intestine; water is absorbed from the fecal contents and the muscular coat undergoes peristaltic contractions. Anything which causes distention of the lumen of the appendix, or which causes a very forceful peristalsis, causing pain which is referred to an area around the umbilicus. Some etiological factors are adhesions, hypertrophied lymphoid tissue near the outlet of the appendix blocking the lumen, or even a Lane's kink involving the appendix. Appendiceal colic may be present over a period of years, and in these cases appendicitis only develops as a pathological change primarily in the mucous membrane as a result of obstruction.

—A. JOHNSTON, '40.

Book Reviews

A METHOD OF ANATOMY, DESCRIPTIVE AND DEDUCTIVE

By J. C. BOILEAU GRANT, M.C., M.B., Ch.B., F.R.C.S. (Edin.)
Professor of Anatomy, University of Toronto.

(650 pp., Illustrated, Indexed, $6.00. William Wood & Co., Baltimore, 1937.)

For some years there has been a steadily growing feeling that a need exists for some new method of presentation of gross anatomy. The standard textbooks, while of unimpeachable excellence from the standpoint of authoritative content, are nevertheless somewhat dull and uninspired from the standpoint of method of presentation. Professor Grant has attempted to solve this difficulty in presenting a new "Method of Anatomy".

On the whole this volume is a definite and creditable achievement. It is interesting and informative, and is well illustrated by a large number of simple, but cleverly executed, drawings. It has definite style and many parts of the subject matter are enlivened by the author's personal inspiration. There are points of detail which might be criticized, but one hesitates to particularize on a work which by and large merits nothing but praise.

There is one difficulty in the use of this book which one foresees. It does not replace the standard texts for the student who approaches the subject for the first time. Nor is it an applied text which gives the clinical student all he requires. It is excellent supplementary reading for the course in anatomy, and it is an extremely valuable book for purposes of review. As a whole it is definitely a worthwhile contribution, and a welcome addition to any medical library.

—H. A. SKINNER, M.B., F.R.C.S. (C.)

HISTOPATHOLOGY OF SKIN DISEASES

By LEE MCCARTHY, M.D., *Associate Clinical Professor of Dermatology, Georgetown University Medical School.*

(First Edition, 513 pp., Illustrated, $18.00. C. V. Mosby Company, St. Louis, 1931.)

This well-known book is probably the best, and only one, of its kind in the English language. The histology of skin diseases has become a very important part of dermatology. Biopsies of skin lesions, now frequently employed, in many instances add knowledge of a definite and specific nature, thus assisting in establishing an accurate diagnosis. It

must, however, be remembered that some skin diseases give no specific microscopic picture. The book is profusely illustrated with drawings and photomicrographs of a very high standard. The author has classified the skin diseases on a histological basis. The subject matter is compiled and written in such a manner as to make it easy to read and follow. The book is highly recommended for both practitioners of medicine and medical students.

—J. H. FISHER, M.D., M.Sc., F.R.C.P. (C.)

PRACTICAL NEUROANATOMY

By J. H. GLOBUS, B.S., M.D., *Associate Professor of Neuroanatomy, New York University, and Assistant Clinical Professor of Neurology, Columbia University.*

(387 pp., 367 Illustrations, Indexed, $6.00. William Wood & Co., Baltimore, 1937.)

Practical Neuroanatomy, by Globus, is a departure from the usual type of textbook of neuroanatomy. The subject matter is orthodox and adds little to our knowledge of the anatomy of the central nervous system. The method of presentation, however, departs sufficiently from that of the standard texts to render this book a welcome addition to our medical library.

The needs of the student during an elementary course such as is presented to students of medicine are covered. Part I of the text consists of twenty-five laboratory assignments. The section dealing with each assignment includes brief instructions for the dissection of the area, with a list of the more important structures to be studied. There follows in each case a fairly detailed description of the area under consideration. Part II of the text consists of twelve chapters dealing with general topics which are not considered systematically during the dissection. These chapters serve the useful purpose of correlating the information acquired during the first hand observation of the material.

Several clinical examples are presented which illustrate the method of application of neuroanatomical knowledge in clinical neurology.

The most commonly used neurohistological techniques are briefly described.

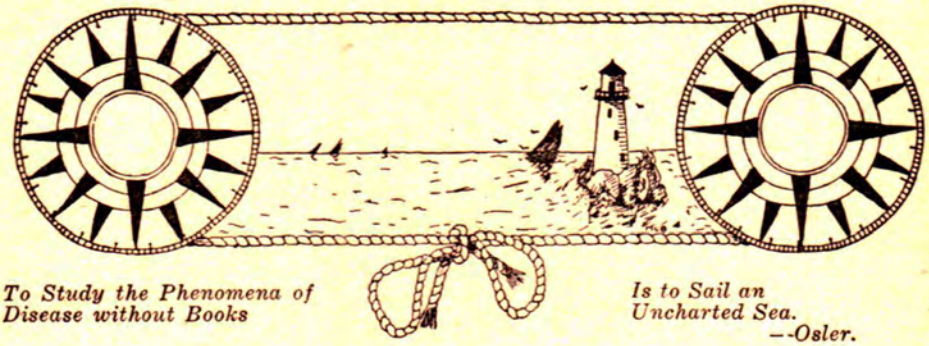
A feature of Globus' book is the inclusion of fifty-five outline drawings on perforated sheets. These are to be filled in with coloured pencils during the progress of the laboratory course. The sheets may be removed while they are being used in the laboratory, and pasted in the book upon their completion.

Practical Neuroanatomy is printed in good type, on good quality paper, and is well bound. The illustrations are quite satisfactory.

While the book should receive a favourable reception, there is one criticism which should be mentioned. The same criticism could be made not only of Globus' text, but also of the majority of the current textbooks on neuroanatomy. The anatomical facts are presented with very little regard to their functional significance. The reviewer is strongly

of the opinion that special treatises dealing with the structure of the central nervous system should ignore the boundaries of strict morphology and present the subject matter from the functional standpoint. This can be done without encroaching upon the domain of neurophysiology. This matter is of particular importance to the student of medicine, for an understanding of the living, dynamic central nervous system must precede any attempt to learn the intricacies of aberrant neurological behaviour.

—M. L. BARR, M.D.



To Study the Phenomena of Disease without Books

Is to Sail an Uncharted Sea.
—Osler.

RECENT ACCESSIONS TO THE MEDICAL SCHOOL LIBRARY

Bainbridge & Menzies: Essentials of Physiology; 8th ed., 1936.
Branhill: Surgical Anatomy of the Head and Neck; 1937.
Chambers: The Conquest of Cholera, America's Greatest Scourge; 1938.
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Editorial

WHEN a student, just out of preparatory school, chooses Medicine as a profession, he ordinarily picks his school for one of two reasons. He goes to the school from which his father or family physician graduated or, for economical reasons, he goes to the school nearest his home. Fortunately, undergraduate medical education on this continent is comparatively well standardized, so that this hit-or-miss type of choice does not influence greatly his future chance of success in his chosen profession. However, from the time that the medico receives his sheepskin, further education ceases to be standard, and must be best suited to fill individual needs.

Unfortunately, the choice of an interneship for further education is too often governed by the same type of hit-or-miss methods. It is true that certain bulletins are published by hospitals, and that deans of medical schools have a certain amount of information for the graduating student but these sources have proved, altogether too often, to be inadequate.

At the first conference of the Canadian Association of Medical Students and Internes, a need was felt for a centralized bureau of information for graduating students. Thus, in a report of the first conference of the C. A. M. S. I., under the purposes of the organization, is found this section:

(d) Interne Appointments—

1. Attempt to solve the present confusion frequently attending the appointment of internes in the interest of internes as well as the hospitals.
2. Co-operation with the Department of Hospital Service in evolving a more definite and broader prospectus of interne appointments, based in part on reports from past internes.

The above is only one of the many purposes of the C. A. M. S. I. Under the capable leadership of Mr. P. F. McGoey, of the University of Toronto, this organization is expecting to achieve much in the way of improvement of the life of the student and the interne. However, the whole-hearted support of students and graduates is needed for success. We hope our students and our graduates will do all they can to assure the success of such an important movement.

—H. A. K.

Abstracts

LAXATIVES AND BOWEL CONSCIOUSNESS

By M. KRAEMER

Am. J. Dig. Dis.; 5:9, 1938

This discussion does not refer to constipation arising from organic obstruction of the bowel, or from spinal cord disease. The author believes that constipation as a disease entity does not exist, but is rather a symptom arising in the patient's mind, and the use of laxatives is evidence of bowel consciousness rather than constipation. A study of the habits of 300 patients as regards laxatives is presented. The etiological factors of bowel consciousness may be advertising, the physician, or friends. The physician is often culpable by showing too much concern over the regularity of fecal movements, by routinely prescribing laxatives postoperatively or to pregnant women, by treating constipation as a serious disease, or by being influenced by advertising. The author recommends that the condition be treated by the education of parents against laxatives, more guarded prescribing of laxatives by the physician and by legislation to curb the flood of advertising.

—N. MCNALLY, '40.

TUBERCULOSIS IN CHILDREN

By J. SIDBURY

South. Med. J.; 30:769, 1937

Usually the symptoms are only mild and the disease needs no specific treatment. The patient is usually allowed to follow the activities of other children of the same age, but strenuous exercise should be avoided and the patient should take a rest every afternoon. If the primary lesion is in the inflammatory stage or if there are caseous lymph glands and fever, sanitarium treatment is desirable. The fibrocaseous type of pulmonary tuberculosis is not common in children and is treated in a similar manner to that occurring in adults. If the home conditions are not optimal it is best to place children suffering from active tuberculosis in a preventorium.

—H. KESTER, '40.

HYSTERICAL BLINDNESS IN CHILDREN

By E. WOLFF AND G. LACHMAN

Am. J. Dis. Children; 55:743, 1938

Hysterical amblyopia is usually bilateral, occurs most commonly in young females, may be transitory or persist for months and can be diagnosed only by the exclusion of organic disease of the ocular or nervous systems. The characteristic finding is a tubular field of vision which does not increase in size for distant objects, the field for colour is usually contracted more than that for white light. The child has usually witnessed the attention given to a friend who has had ocular disturbances, and there is often the history of an emotional upset, frequently the loss of a friend. Cases of short duration respond more quickly to treatment which consists of friendliness, instillation of confidence in the treatment, and psychotherapy.

A. CONLEY, '40.

A CONSTRUCTIVE CRITICISM OF CERTAIN HOSPITAL PROCEDURES

By K. BOWMAN

Am. J. Psychiatry; 94:1141, 1938

The author suggests several revisions of hospital routine. He suggests that patients be allowed to sleep the morning after having had a sedative, in order to allow the maximum effect from the drug. He further believes that hospital hours for rising and meal times should be more in accord with those of the patient's normal life. He also advocates that patients be allowed to lie on their beds during the daytime, feeling that the rest so obtained is more valuable than the appearance of a neat bed. He advises the same attitude toward women smoking should be adopted as for men. A cigarette is better than a sedative, and the refusal only creates further difficulties. He greatly stresses the need of twenty-four-hour use of the continuous water baths, or if used only half the day they should be used at night when most needed rather than during the day.

—R. BOURNE, '38.

THE TREATMENT OF THE INDIVIDUAL IN THE CARE OF PEPTIC ULCER

By J. MEYER AND J. KASANIN

Am. J. Dig. Dis.; 5:12, 1938

At the Mandel Clinic, with which the authors are associated, all examinations of patients with peptic ulcer take the form of conferences, the internist, psychiatrist, physiologist and social worker participating, not only in the analysis of each case but also in the treatment. The treatment consists of the ordinary hygienic re-education of the patient with reference to rest, relaxation and divided food intake, but also includes a correction of those environmental factors which lead to mental strain. In those cases in which the patient has developed a definite neuroses, psychoanalysis is of use. An outline of their method of treatment is presented. The system has brought gratifying results, and two cases are cited as examples of the efficacy of intelligent evaluation of the patient, in those cases where the deciding factors in the amelioration of symptoms were psychological and sociological rather than medical.

—N. MCNALLY, '40.

OBSERVATIONS ON THE ETIOLOGY OF ABRUPTIO PLACENTAE AND ITS RESPONSE TO VITAMIN E THERAPY

By E. SHUTE

J. Ob. Gyn. Br. Emp.; 44:121, 1937

The discussion is based on the clinical observations made on a series of miscarriages and abortions. A description of the clinical picture is given, the most constant symptom being the gradual appearance of a restricted palm-sized area of true uterine tenderness accompanied by steady sacral backache. From experimental evidence it was thought that the etiological factor might be an imbalance between the vitamin E and the oestrogenic substance of the blood serum. In 65 cases showing this clinical condition 75 per cent showed an excess of oestrogenic substance in the blood serum. Adequate doses of vitamin E has completely cured this condition in almost all cases. The author thinks that vitamin E is of definite therapeutic value in cases of abruptio placentae, and suggests that adequate dosage with a potent vitamin E from the beginning of pregnancy might reduce the incidence of abruptio placentae.

—O. LOCKHART, '39.

THE DIAGNOSIS OF DRUNKENNESS

By E. MCCORMICK

Practitioner; 140:627, 1938

The diagnosis of drunkenness rests on the accumulation of signs and symptoms from the affected organs of the body. There is no scientific definition of drunkenness, but the diagnosis is often of medico-legal importance. The pulse is full and bounding at first, but as collapse comes on it becomes weak and thready. Blood pressure is almost always increased about 20 mm. Hg., while in shock the blood pressure is low. The effects of alcohol on the nervous centres are manifold, but cerebration is usually slow and uncertain, the patient's manner and general conduct are important. There is often lack of muscular control as tested for by writing. Speech may be slurring or otherwise affected. Cerebellar dysfunction is best tested for by having the patient walk to one end of the room, turn sharply and return, rather than by walking a straight line. Rhomberg's sign is of medico-legal importance. Ocular signs include conjunctivitis, often mydriasis, the reaction to light is sluggish. The ability of the patient to conduct himself in a normal manner is most important.

—K. CALVERT, '39.

MALIGNANT TUMOUR OF THE THYMUS GLAND

By R. EVANS

The author presents a case of malignancy of the thymus gland which occurred in a boy five years of age, and which in many respects resembled acute pulmonary tuberculosis. At autopsy, the tumour was found to be a malignant lymphoma composed of undifferentiated cells resembling small lymphocytes, and which had invaded the heart, left lung and pleura, but not the pericardium or the arch of the aorta. The thymus is rarely the site of either primary or secondary neoplasms, the commonest type being a primary tumour which is considered to be a round cell sarcomma or a lymphosarcomma. The symptoms are very variable, and diagnosis is difficult or even impossible. Because of the involvement of the great vessels, the tumour mass cannot be excised surgically and the use of X-ray therapy is of questionable value. The prognosis is bad, the patient usually dying within one year from the onset of symptoms from asphyxia and venous obstruction.

—J. GALLOWAY, '40.

THE EFFECT ON DONORS OF REPEATED BLOOD LOSS

By F. CADHAM

Can. Med. Assn. J.; 38:465, 1938

Six months after having given repeated small blood transfusions the physical condition of 125 donors was investigated. None of the donors reported any ill effects, but most reported that they were improved in health, 65 donors noted an improvement in appetite, and there were reports of the disappearance of acne pustules and urticarial attacks. There was in no case a change in the blood volume or in the concentration of complement in the blood serum. No explanation of the beneficial effects of repeated blood-letting is offered, but it is suggested that it may be of some therapeutic value.

—R. STOREY, '39.

CLINICAL AND EXPERIMENTAL STUDIES WITH NON-INVAGINATION OF THE APPENDICEAL STUMP

By J. DONALDSON AND H. THATCHER

Southern Med. J.; 31:83, 1938

The authors report the results of an experimental study of appendectomy on 82 dogs. In 26 dogs the stump of the appendix was invaginated with a black silk purse string suture, in 30 the stump was left free in the peritoneal cavity and in 26 the stump was buried with a chromic catgut #0 suture. They found that complications such as adhesions, fecal fistulae, peritonitis, or local abscess were less frequent when the stump was invaginated, and that invagination with black silk was preferable to invagination with chromic catgut. The authors state that the non-invagination method is only to be preferred in cases in which the appendix is remotely placed and when the serosa has become thickened and fragile as a result of considerable local peritonitis.

—D. STATE, '39.

SMALLPOX VACCINE IN THE TREATMENT OF RECURRENT HERPES SIMPLEX

By P. FOSTER AND A. ABSHIER

Arch. Dermat. and Syph.; 36:294, 1937

The authors give an excellent discussion of the virus theory of the etiology of herpes simplex. Experimentally they showed that the virus of smallpox was very closely related antigenically to that of herpes simplex, the relationship resembling that between smallpox and cowpox, or between chickenpox and herpes zoster. Herpes zoster and herpes simplex were in no way related clinically or etiologically. Experimentally it was possible to produce an immunity to herpes simplex in animals by an inoculation with the virus, but an attack of herpes simplex in man does not give a sufficient immunity to prevent a recurrence of the condition. Vaccination was performed four times at intervals of two weeks, unless a "take" was observed, on 35 patients. There was a 14% recurrence of herpes simplex in two years. The action of the smallpox vaccination is to raise the antibody titre above that level which will allow an invasion with the virus. The treatment can also be used to shorten an attack of herpes simplex.

—R. CRAM, '41.

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